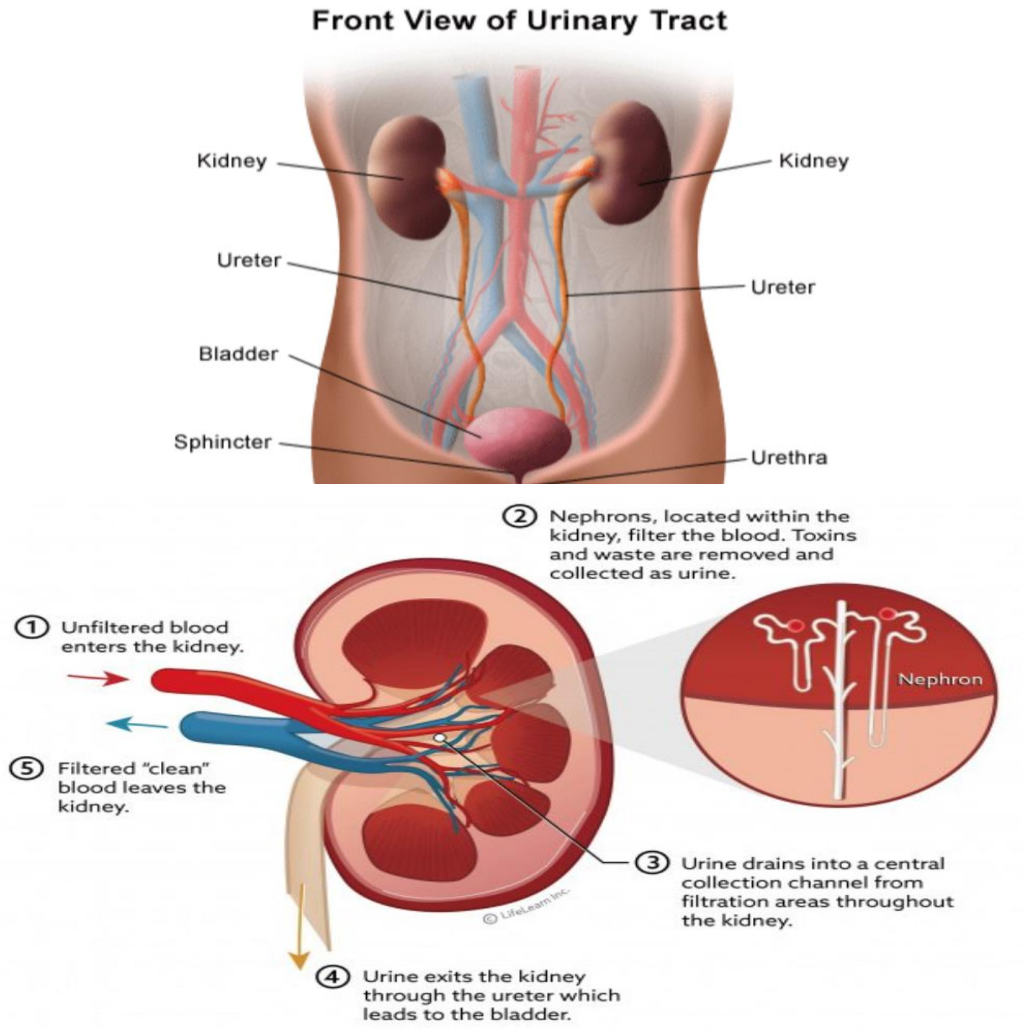
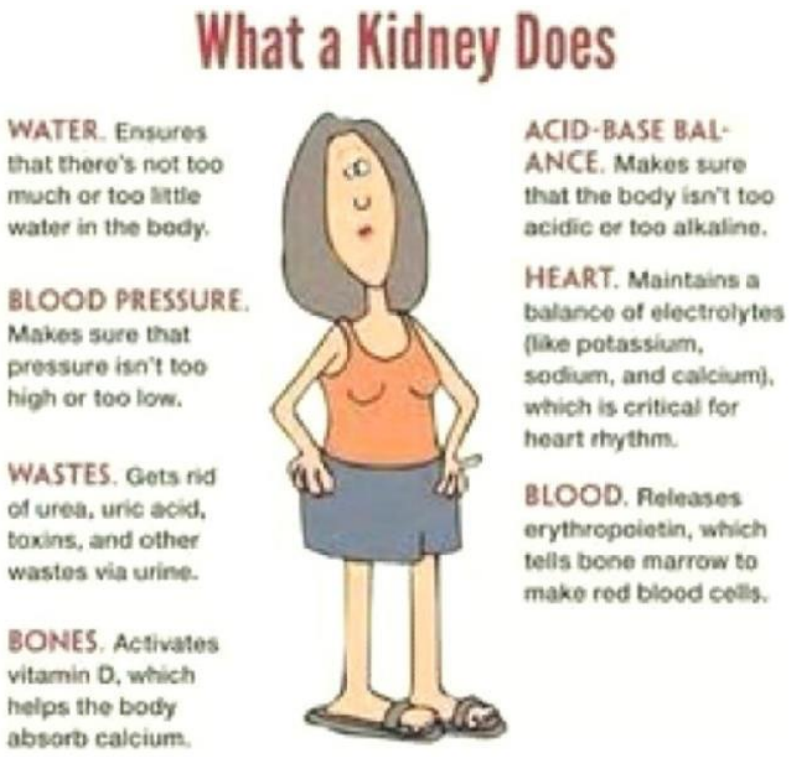
Lecture.8 Presenting problems in renal and urinary tract disease





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Need Some Help?

Loin pain

Loin pain is often caused by ***musculoskeletal*** disease but can be a manifestation of ***renal*** tract disease; in the latter case, it may arise from renal stones, ureteric stones, renal tumours, acute pyelonephritis and urinary tract obstruction. Acute loin pain radiating anteriorly and often to the groin is termed renal colic. When combined with haematuria, this is typical of ureteric obstruction due to calculi .

Dysuria

Dysuria refers to painful urination, often described as burning, scalding or stinging, and commonly accompanied by suprapubic pain. It is often associated with frequency of micturition and a feeling of incomplete emptying of the bladder. By far the most common cause is urinary tract infection. Other diagnoses that need to be considered in patients with dysuria include sexually transmitted infections and bladder stones .

Frequency

- Frequency describes daytime micturition more often than a patient would expect. It may be a consequence of polyuria, when urine volume is normal or high, but is also found in patients with dysuria and prostatic diseases, when the urine volume is normal.

Polyuria

- Polyuria is defined as a urine volume in excess of 3 L/24 hrs. Various underlying conditions, both renal and extrarenal, may be responsible. Investigation of polyuria includes measurement of urea, creatinine and electrolytes, glucose, calcium and albumin. A 24-hour urine collection may be helpful to confirm the severity of polyuria. The presence of nocturnal polyuria suggests a pathological cause.

15.13 Causes of polyuria

- Excess fluid intake
- Osmotic diuresis: hyperglycaemia, hypercalcaemia
- Cranial diabetes insipidus
- Nephrogenic diabetes insipidus:
  - Rare inherited mutations in vasopressin receptor or aquaporin 2 genes
  - Lithium
  - Diuretics
  - Interstitial nephritis
  - Hypokalaemia
  - Hypercalcaemia

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Nocturia

- Nocturia is defined as waking up at night to void urine. It may be a consequence of polyuria but may also result from increased fluid intake or diuretic use in the late evening (including caffeine). Nocturia also occurs in CKD, and in prostatic enlargement when it is associated with poor stream, hesitancy, incomplete bladder emptying, terminal dribbling and urinary frequency due to partial urethral obstruction . Nocturia may also occur due to sleep disturbance without any functional abnormalities of the urinary tract.

Urinary incontinence

- Urinary incontinence is defined as any involuntary leakage of urine. It may occur in patients with a normal urinary tract, as the result of dementia or poor mobility, or transiently during an acute illness or hospitalisation, especially in older people.

types:

1- **Stress** : [bladder pressure exceeds the urethral pressure] , either due to weak pelvic floor muscles or weak urethral sphincter.

incont. During coughing , sneezing , straining . more in women.

2- **Urge** : detrusor overactivity [bladder pressure > urethral sphincter]

Occur more in elderly (> 65 y) , with some neurological conditions .

3- **Continual**: suggestive of fistula (after surgery or radiotherapy) may occur with advanced stress incontinence.

4–**Overflow** : with chronically over distended bladder .

Either by bladder outflow obstruction or detrusor muscle failure (atonic bladder)

Oliguria/anuria

Oliguria: less than 400 mL of urine is passed per day, **anuria:** less than 100 mL of urine is passed per day. Urine volume alone is a poor indicator of the severity of kidney disease. Oliguria and anuria may be caused by a reduction in urine production, as in pre-renal AKI, when GFR is reduced and tubular homeostatic mechanisms increase reabsorption to conserve salt and water.

Obstruction of the renal tract can produce oliguria and anuria, but to do so, obstruction must be complete and occur distal to the bladder neck, be bilateral, or be unilateral on the side of a single functioning kidney.

Partial obstruction can be associated with a normal or even high urine volume due to chronic tubular injury, which causes loss of tubular concentrating ability.

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15.6 Causes of anuria (<100 mL urine output per day)

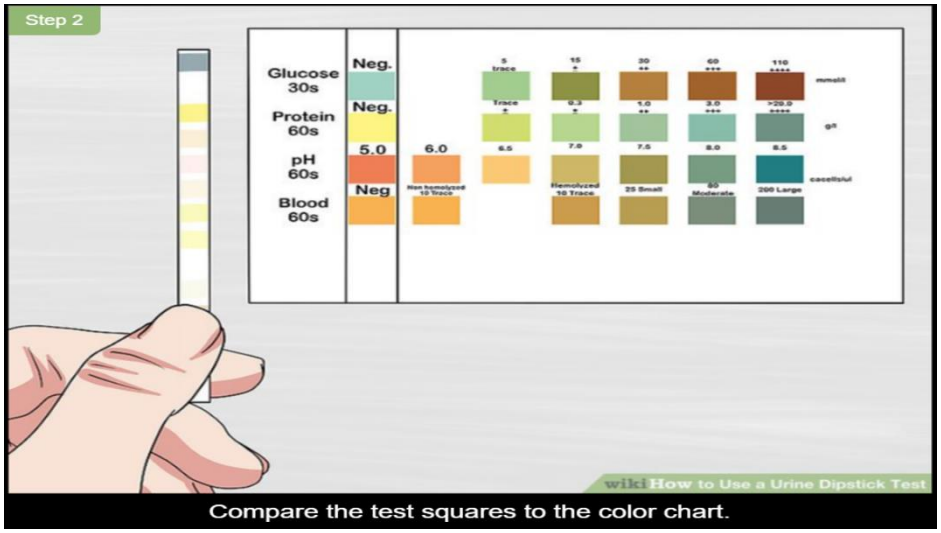
Condition	Examples
Urinary obstruction (complete)	Urinary retention due to prostatic enlargement, urethral stenosis, bladder tumour Bilateral ureteric obstruction due to retroperitoneal fibrosis, cancer, radiation injury Bilateral renal stones (usually staghorn calculi) Massive crystalluria obstruction of tubules (rare)
Lack of renal perfusion (bilateral)	Aortic dissection involving renal arteries Severe acute tubular necrosis Severe functional hypoperfusion (cardiorenal, hepatorenal)
Rapidly progressive glomerulonephritis	Anti-glomerular basement membrane disease, severe antineutrophil cytoplasmic antibody (ANCA) vasculitis (100% glomerular crescents on biopsy)

Hypertension

- Hypertension is a very common feature of renal disease. Additionally, the presence of hypertension identifies a population at risk of developing CKD and current recommendations are that hypertensive patients should have renal function checked annually. Control of hypertension is very important in patients with renal impairment because of its close relationship with further decline of renal function and because of the exaggerated cardiovascular risk associated with CKD.

Haematuria

- Healthy individuals may have occasional red blood cells in the urine (up to 12 500 cells/mL), but the presence of visible (macroscopic) haematuria or non-visible haematuria (microscopic, only detectable on dipstick testing) is indicative of significant bleeding from somewhere in the urinary tract .



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Visible haematuria is most likely to be caused by tumour, which can affect any part of the urogenital tract. Other common causes of visible haematuria are urine infection and stones. Visible haematuria may also be encountered in patients with IgA nephropathy, typically following an upper respiratory tract infection.

Non-visible haematuria may also indicate an underlying tumour, and all patients over 40 years old with persistent (detected on at least 2 of 3 consecutive dipstick tests) non-visible haematuria should therefore undergo imaging and cystoscopy. In younger patients, an underlying tumour is much less likely, and if aglomerular cause is not suspected (see below), it may be appropriate to manage them by periodic observation in primary care.

Glomerular bleeding occurs when inflammatory, destructive or degenerative processes disrupt the GBM, permitting passage of red blood cells into the urine. A characteristic feature of glomerular bleeding is an 'active urinary sediment' (the presence of dysmorphic red blood cells or red cell casts on microscopy); this is not always present, however.

15.7 Interpretation of non-visible haematuria

Dipstick test positive	Urine microscopy	Suggested cause
Haematuria	White blood cells	Infection
	Abnormal epithelial cells	Tumour
	Red cell casts Dysmorphic erythrocytes (phase contrast microscopy)	Glomerular bleeding*
Haemoglobinuria	No red cells	Intravascular haemolysis
Myoglobinuria (brown urine)	No red cells	Rhabdomyolysis

*Glomerular bleeding implies that the GBM is ruptured. It can occur physiologically following very strenuous exertion but usually indicates intrinsic renal disease and is an important feature of the nephritic syndrome.

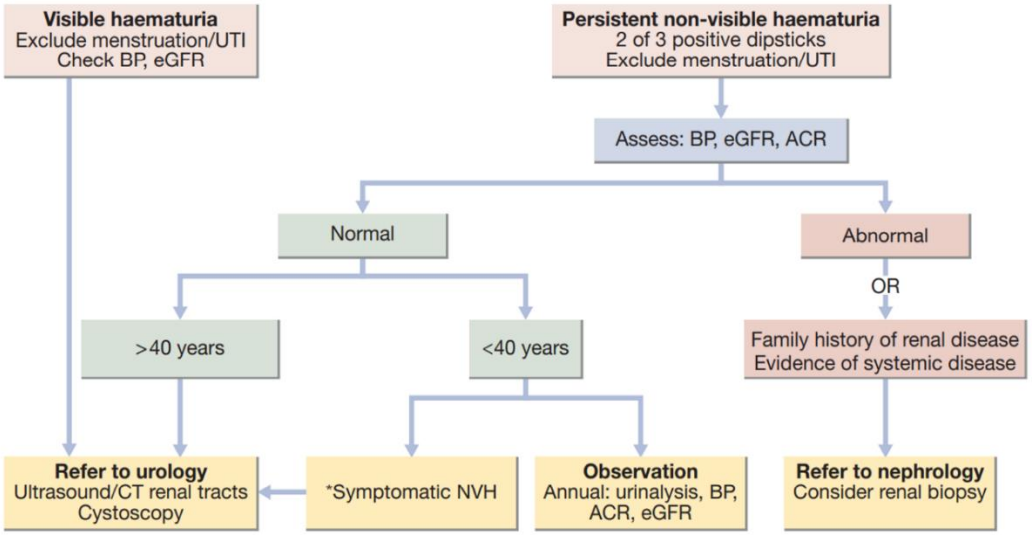

Fig. 15.8 Investigation of haematuria. *Symptomatic: lower urinary tract voiding symptoms such as hesitancy, frequency, urgency and dysuria. (ACR = albumin:creatinine ratio; BP = blood pressure; CT = computed tomography; eGFR = estimated glomerular filtration rate; NVH = non-visible haematuria; UTI = urinary tract infection)

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Proteinuria

- While very small amounts of high-molecular-weight proteins and moderate amounts of low-molecular-weight proteins pass through the healthy GBM, these proteins normally are completely reabsorbed by receptors on tubular cells. Hence, in healthy individuals, less than 150 mg of protein is excreted in the urine each day, much of which is derived from tubular cells.
- The presence of larger amounts of protein is usually indicative of significant renal disease.

Proteinuria is usually asymptomatic and is often picked up by urinalysis, although large amounts of protein may make the urine frothy. *Transient proteinuria* can occur after vigorous exercise, during fever, in heart failure and in people with urinary tract infection. Testing for proteinuria is best done on an early morning sample, as some individuals exhibit orthostatic proteinuria. In these patients, typically less than 1 g/24 hrs of protein is excreted only in association with an upright posture, the first morning sample being negative. Orthostatic proteinuria is regarded as a benign disorder that does not require treatment.

Moderately elevated albuminuria(microalbuminuria)

May indicate early glomerular pathology, at a time when the standard dipstick test remains negative . Screening for moderately elevated albuminuria should be performed regularly in patients with diabetes, as persistently elevated levels warrant therapy with inhibitors of the renin–angiotensin–aldosterone system, even in normotensive individuals, to reduce the rate of loss of renal function. Persistent moderately increased albuminuria has also been associated with cardiovascular mortality in patients with and without diabetes.

Overt (dipstick-positive) proteinuria

- Typically, standard dipsticks test positive for protein once the urinary protein exceeds approximately 0.5 g/24 hrs; however, trace to 1+ on dipstick may be observed in very concentrated urine from individuals with no evidence of renal pathology. Hence all patients with persistent proteinuria on dipstick should have the amount of protein quantified to guide further investigations . When more than 1 g of protein per day is being excreted, glomerular disease is likely and this is an indication for renal biopsy.

Since quantification by 24-hour urine collection is often inaccurate, the protein:creatinine ratio (PCR) in a spot sample of urine is preferred. It is possible to measure albumin:creatinine ratio (ACR), but this requires a more expensive immunoassay and is

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usually reserved for situations when high sensitivity is required, such as detection of the early stages of diabetic nephropathy.

15.9 Quantifying proteinuria in random urine samples

ACR[1]	PCR[2]	Typical dipstick results[3]	Significance
<3.5 (female) <2.5 (male)	<25	–	Normal
3.5–30	25–50	–	Moderately elevated albuminuria
30–70	50–100	+ to ++	Dipstick positive
70–300	100–350	++ to +++	Glomerular disease more likely; equivalent to >1 g/24 hrs
>300	>350	+++ to ++++	Nephrotic range: almost always glomerular disease, equivalent to > 3.5 g/24 hrs

[1]Urinary albumin (mg/L)/urine creatinine (mmol/L). [2]Urine protein (mg/L)/urine creatinine (mmol/L). (If urine creatinine is measured in mg/dL, reference values for PCR and ACR can be derived by dividing by 11.31.) [3]Dipstick results are affected by urine concentration and are occasionally weakly positive on normal samples.

It is sometimes helpful to identify the type of protein in the urine. Large amounts of low-molecular-weight proteins, such as β2-microglobulin (molecular weight 12 kDa), in the urine suggest renal tubular damage and are referred to as tubular proteinuria. This rarely exceeds 1.5–2 g/24 hrs (maximum PCR 150–200 mg/ mmol.

Free immunoglobulin light chains (molecular weight 25 kDa) are filtered freely at the glomerulus but are poorly identified by dipstick tests. Hence, electrophoresis of the urine and specific immunodetection methods are required to detect immunoglobulin light chains, known as ‘Bence Jones protein’. This may occur in AL amyloidosis and in B-cell dyscrasias but is particularly important as a marker for myeloma .

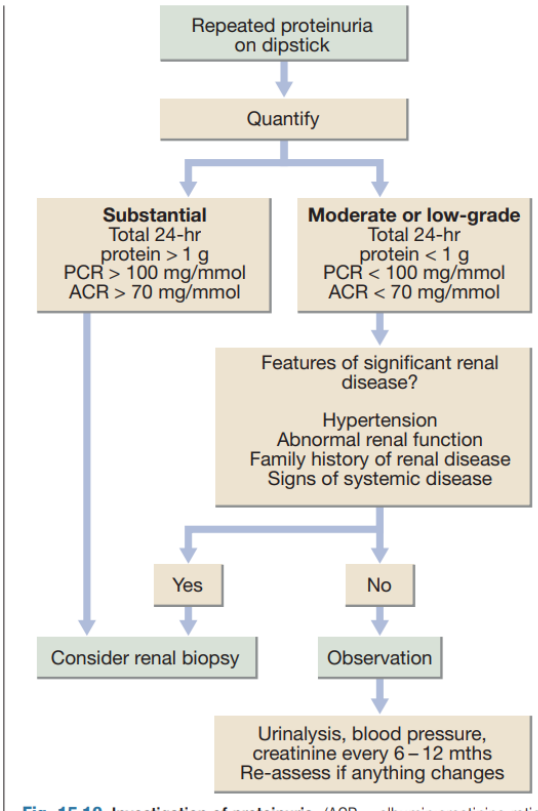

Fig. 15.10 Investigation of proteinuria. (ACR = albumin:creatinine ratio; PCR = protein:creatinine ratio.)

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