BMJ Best Practice

# Assessment of proteinuria

The right clinical information, right where it's needed


Last updated: Jul 29, 2016

# Table of Contents

# Summary


◊ Average daily urinary protein excretion in adults is 80 mg/day, with normal excretion considered to be <150 mg/day. Albumin represents approximately 15% of the daily urinary protein excretion in healthy people, with other plasma proteins (e.g., immunoglobulins, beta-2-microglobulin) and Tamm-Horsfall protein constituting the remaining 85%. Proteinuria varies in amount and may be transient or persistent.[1] [2]

Urinary excretion of abnormal quantities of protein for ≥3 months, with or without a decrease in glomerular filtration rate (GFR), is diagnostic of chronic kidney disease.[3] [4]

Urine albumin measurement is an important component in screening for chronic kidney disease. The presence of proteinuria is an independent risk factor for cardiovascular disease, death, and end-stage renal disease in the general population, and in patients with chronic kidney disease.[5] [6] [7] [8] [9] Presence of proteinuria is associated with a higher mortality in critically ill patients;[10] [11] the degree of proteinuria post renal transplantation is predictive of graft and patient survival.[12]

Reduction of proteinuria by pharmacological therapy is used as a surrogate marker in the management of chronic kidney disease and many acute glomerular diseases and is associated with improved renal outcomes.[13] [14] [15] [16] [17] [18] [19]

◊ **Proteinuria definitions :**
Either total urine protein or just the albumin fraction can be measured. Urine albumin measurements are better validated in regard to association with risk for chronic kidney disease progression and cardiovascular events.

Albuminuria

Albuminuria is graded as follows:[20]

- A1 (normal to mildly increased albuminuria)
  - Albumin excretion rate: <30 mg/24 hours.
  - Albumin-to-creatinine ratio (ACR): <30 mg/g.
- A2 (moderately increased albuminuria)
  - Albumin excretion rate: 30-300 mg/24 hours.
  - Albumin-to-creatinine ratio (ACR): 30-300 mg/g.
  - Associated with increased risk of progressive kidney disease and cardiovascular events.
- A3 (severely increased albuminuria)
  - Albumin excretion rate: >300 mg/24 hours.
  - Albumin-to-creatinine ratio (ACR): >300 mg/g.
  - Larger amounts of proteinuria are associated with worse renal survival. These patients should be referred to a nephrologist.

Nephrotic range proteinuria

- Urine total protein: ≥3.5 g/day.
- The presence of nephrotic-range proteinuria with oedema, hypoalbuminaemia (<3.0 g/dL), and hyperlipidaemia is defined as nephrotic syndrome.

Glomerular proteinuria

- Urine total protein: 1-20 g/day.
- Passage of protein from glomerular capillary blood (mainly albumin) into the urine.

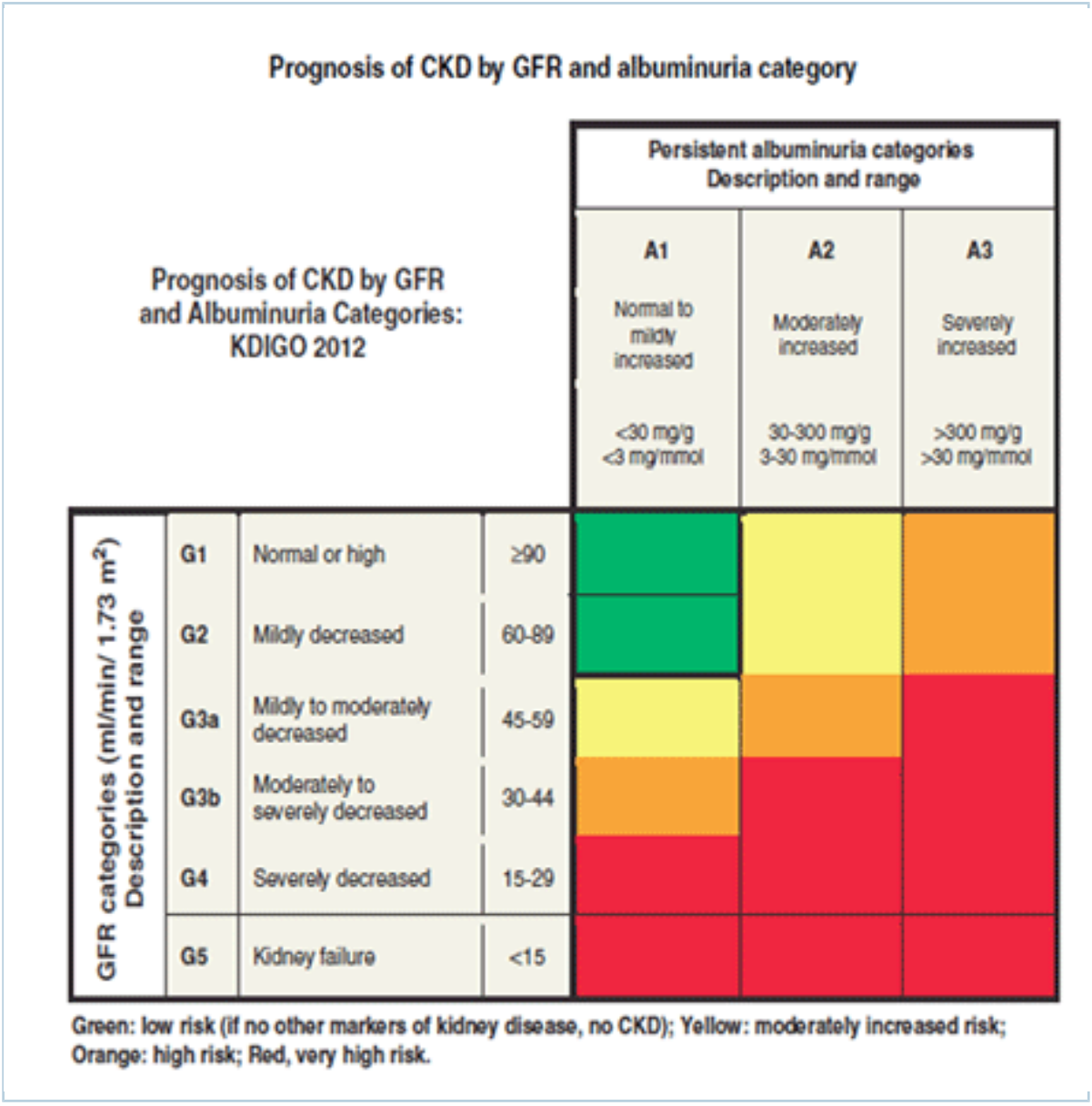
Tubular proteinuria

- Urine total protein: <2 g/day.
- Passage of low molecular weight proteins (e.g., retinol-binding protein, alpha-2-microglobulin, beta-2-microglobulin) into the urine.

Overflow proteinuria

- Urine total protein: up to 20 g/day.
- Overproduction of small proteins (e.g., myoglobin, light chains) leads to increased glomerular filtration and appearance in the urine.

◊ **Effect of albuminuria on prognosis of chronic kidney disease :**
Albuminuria is an independent risk factor for the progression of chronic kidney disease. Severely increased levels of albuminuria in the setting of normal GFR may impart a greater risk for progressive chronic kidney disease than mildly reduced GFR with normo-albuminuria.




*Prognosis of CKD by GFR and albuminuria category: CKD, chronic kidney disease; GFR, glomerular filtration rate; KDIGO, Kidney Disease Improving Global Outcomes*



In patients with advanced CKD, proteinuria is the strongest predictor of time to end-stage renal disease.[21]

◊ **Epidemiology :**
Proteinuria is common, and prevalence increases with kidney disease progression. There is evidence that both moderately and severely increased albuminuria are more common in black people than in white people. As the GFR declines from >90 mL/minute/1.73 m^2 to 15-59 mL/minute/1.73 m^2, the prevalence of moderately increased albuminuria (ACR <300mg/g) increases from 6.0% to 23.2%, and the prevalence of severely increased albuminuria (ACR >300mg/g) increases from 0.6% to 8.6%.[22] Prevalence of moderately increased albuminuria has also been shown to increase with increasing body mass index (BMI). Data from a population screening programme in Sheffield, UK, found that the prevalence increased from 3.1% in those with BMI <25%, to 27.2% in those with BMI >30.[23]

◊ **Detection: qualitative testing :**

- In the laboratory, proteinuria has traditionally been routinely detected through the use of multi-reagent urinary dipstick testing.
- The presence of urinary albumin is detected by a colorimetric reaction with the dipstick-impregnated reagent.
- Dipstick testing has limited sensitivity for non-albumin protein and is therefore often falsely negative in the presence of predominately tubular or overflow proteinuria.
- The sensitivity of the urinary dipstick for albumin ranges from 83% to 98% with a specificity of 59% to 86%.[24] [25] This reaction depends on the concentration of albumin, so the testing of large-volume, diluted urine underestimates the degree of albuminuria. Similarly, testing highly concentrated urine may overestimate the degree of albuminuria.
- Markedly alkaline pH (>8.0) and administration of iodinated radiocontrast agents can also produce false-positive results.
- Although qualitative dipstick testing is rapid, easy to perform, and commonplace, the false-positive and false-negative rates limit the utility.

| | |
|---|---|
| negative | 0 mg/dL |
| trace | 15-30 mg/dL |
| 1+ | 30-100 mg/dL |
| 2+ | 100-300 mg/dL |
| 3+ | 300-1000 mg/dL |
| 4+ | >1000 mg/dL |

*Dipstick proteinuria ranges*
*Created by BMJ Evidence Centre using author content*

- Physicians should consult the product-specific information for interpretation of the urine dipstick results with a corresponding urine protein level.
- In the past, sulphosalicylic acid (SSA) was added to urine specimens to precipitate all protein, for the detection of non-albumin proteins. The resultant turbidity is graded on a scale from 0 to 4+. Although SSA testing is still used, semi-quantitative and quantitative testing methods have largely replaced it.

◊ **Detection: semi-quantitative testing :**

- Newer dipsticks have been marketed that can report albumin-to-creatinine ratios in the microalbumin range, as well as total protein-to-creatinine ratios.
- Standardising the protein measurement to the quantity of creatinine in the urine helps to avoid errors introduced by diluted or concentrated urine samples.
- Measuring total protein also allows detection of tubular and overflow proteinuria. The reported sensitivity of these semi-quantitative dipsticks is 80% to 97% with a specificity of 33% to 80%.[26]

◊ **Detection: quantitative testing :**

- Quantitative testing of albumin using urine albumin concentration or albumin-to-creatinine ratio is sensitive and specific for detecting albuminuria.[27] [28]
- Measuring urine albumin concentration without measuring urine creatinine concentration is less expensive, and has demonstrated similar sensitivity and specificity as albumin-to-creatinine ratio for screening purposes in diabetics.[28]
- Twenty-four-hour urine collections have traditionally been used, although these collections are prone to over- and under-collection. Moreover, 24-hour urine collections are cumbersome for patients. Reporting the total 24-hour urine protein standardised to the 24-hour urine creatinine (g protein/g creatinine) helps to adjust for variations in the duration of collection.
- In women an adequate collection typically has 15 to 20 mg of creatinine per kg of body weight, and in men 20 to 25 mg/kg.
- Alternatively, the expected grams of excreted creatinine can be estimated by 140 minus age multiplied by weight/5000 [(140 - age) x weight/5000], where weight is in kilograms. This result is multiplied by 0.85 in women.[29]
- More commonly, a urine protein-to-creatinine ratio or albumin-to-creatinine ratio on a spot urine sample is used to approximate the 24-hour urine protein excretion and 24-hour urine albumin excretion, respectively.
- Albumin to creatinine ratio is more sensitive than protein to creatinine ratio in detecting low levels of proteinuria.[30]
- A first morning sample most closely estimates 24-hour protein excretion, although a random sample is acceptable if a first morning void is unavailable.[3] [29] [31]
- Because of diurnal variation, it is best to collect spot urine samples at the same time each day if being used to follow up patients long term. Additionally, the correlation of the spot sample with 24-hour excretion is less robust with nephrotic-range proteinuria. The spot ratio may also be less accurate in pregnant women with >300 mg of proteinuria.[32] [33]
- People with body surface areas of 1.73 m^2 excrete roughly 1 g of creatinine. As such, a protein-to-creatinine ratio of 1 g protein/g creatinine in an average-sized person approximates 1 g of proteinuria in 24 hours. It is important to recognise that a ratio of 2.5 g protein/g creatinine in a muscular person who excretes 2 g of creatinine in 24 hours may actually represent nephrotic-range proteinuria of 5 g/day. Similarly, an older, frail woman may excrete <1 g of creatinine per day, and in this setting the spot ratio would overestimate her proteinuria.

# Aetiology

Proteinuria can be transient or persistent. Transient proteinuria can be detected in several clinical scenarios, including after heavy physical exertion, in patients with fever, during urinary tract infection, and in patients with significant urological haemorrhage. Proteinuria can also occur with the assumption of upright posture (orthostatic proteinuria). Transient and orthostatic proteinuria are of little clinical significance.[34] [35] The presence of dipstick-positive proteinuria on 2 urine samples separated by 1 to 2 weeks indicates persistent proteinuria and warrants quantification and further assessment.[3]

## Glomerular

The glomerulus forms a barrier to the filtration of large blood proteins into the urinary space. Disruption or loss of the glomerular basement membrane or podocyte foot process effacement allows protein to pass from glomerular capillary blood into the urine. Because albumin is the major protein in blood, glomerular proteinuria is defined by a predominance of albumin. Proteinuria accompanied by haematuria is more likely to be of glomerular aetiology. Glomerular proteinuria is typically in the range of 1 to 20 g/day. Moderately increased albuminuria is also considered to be of glomerular aetiology, although the absolute quantity does not meet the definition for overt proteinuria. Moderately increased albuminuria is seen in disease processes characterised by endothelial dysfunction (e.g., early diabetic nephropathy, metabolic syndrome, cardiovascular disease) with resultant disruption of the glomerular endothelial lining.

Glomerular causes of proteinuria include diabetic nephropathy, hypertension, metabolic syndrome, minimal change disease, focal segmental glomerulosclerosis, membranous nephropathy, membranoproliferative glomerulonephritis, IgA nephropathy, systemic lupus erythematosus, post-infectious glomerulonephritis, haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura, scleroderma renal crisis, medium- and small-vessel vasculitis, amyloidosis, light and heavy chain deposition diseases, fibrillary/immunotactoid glomerulopathy, proliferative glomerulonephritis with IgG deposition, idiopathic nodular glomerulosclerosis, Fabry's disease, and anti-glomerular basement membrane (anti-GBM) disease (Goodpasture's syndrome).

## Tubular

Low-molecular-weight proteins are freely filtered at the glomerulus. In healthy people, the proximal renal tubules metabolise and reabsorb virtually all of this protein to prevent urinary loss. In the setting of tubular dysfunction, abnormal quantities of low-molecular-weight proteins (e.g., retinol-binding protein, alpha-2-microglobulin, beta-2-microglobulin) may escape metabolism and are excreted in the urine. Tubular proteinuria may accompany other markers of tubular dysfunction (e.g., glucosuria, phosphaturia, proximal renal tubular acidosis), and protein excretion is typically <1.5 to 2 g/day. With predominately tubular proteinuria, the ratio of 24-hour albumin to beta-2-microglobulin excretion is generally in the range of 1 to 13, with the ratio in glomerular proteinuria being >1000.[36] Tubular proteinuria often co-exists with glomerular proteinuria.

Tubular causes of proteinuria include acute tubular injury, interstitial nephritis, urinary tract obstruction, Fanconi syndrome, cystic kidney disease, heavy metal poisoning, hypercalciuria, Dent's disease, and aristolochic acid nephropathy.

## Overflow

Production of abnormal quantities of protein that exceed the re-absorptive capacity of the proximal tubules will result in proteinuria. The classic example is the overproduction of monoclonal light chains in a patient with multiple myeloma. The low-molecular-weight light chains are freely filtered at the glomerulus at a concentration surpassing the re-absorptive capacity of the renal tubules. These light chains are subsequently excreted in the urine. Similar to glomerular proteinuria, the total quantity of proteinuria can reach up to 20 g/day.

Overflow causes of proteinuria include light chain cast nephropathy, rhabdomyolysis, and polymyositis.[37]

# Urgent considerations

(See **Differential diagnosis** for more details)
Although proteinuria is rarely a medical emergency, the presence of certain clinical features may indicate a more serious disease process warranting immediate assessment. New-onset proteinuria with features of systemic disease (e.g., progressive renal dysfunction, other organ system abnormalities) should be assessed as soon as possible.

## Renal vein thrombosis

Patients with nephrotic-range proteinuria and marked hypoalbuminaemia (generally <20 g/L [<2.0 g/dL]) who present with acute renal failure or concern for pulmonary embolism may have renal vein thrombosis. The diagnosis is further suggested by new-onset haematuria, acute flank pain, and increasing proteinuria. Diagnosis can be confirmed by renal ultrasonography, magnetic resonance venography, and traditional venography. Anticoagulation is the mainstay of therapy, with catheter-directed thrombolysis being used in select circumstances.[38] These patients are also at risk of traditional deep venous thrombosis, and appropriate diagnostic efforts should be used as needed.

## Rapidly progressive glomerulonephritis

If haematuria and acute renal failure are present, rapidly progressive glomerulonephritis should be considered. If clinically indicated, diagnostic efforts to assess for aetiologies of acute renal failure (e.g., post-infectious glomerulonephritis, systemic lupus erythematosus, membranoproliferative glomerulonephritis, IgA nephropathy, thrombotic microangiopathy, anti-glomerular basement membrane disease, anti-neutrophil cytoplasmic antibody [ANCA]-associated vasculitis) should be made immediately. This may include appropriate serological testing and renal biopsy. Failure to diagnose a rapidly progressive glomerulonephritis may lead to irrecoverable loss of kidney function, morbidity, and even death.

# Red flags

- Urological haemorrhage
- Minimal change disease
- Focal segmental glomerulosclerosis
- Membranous nephropathy
- Membranoproliferative glomerulonephritis
- IgA nephropathy
- Systemic lupus erythematosus
- Post-infectious glomerulonephritis
- Amyloidosis
- Light and heavy chain deposition diseases
- Fibrillary and immunotactoid glomerulopathy
- Anti-glomerular basement membrane (anti-GBM) disease (Goodpasture's syndrome)
- Acute tubular injury
- Interstitial nephritis

- Fanconi syndrome
- Light chain cast nephropathy
- Urinary tract obstruction
- Diabetic nephropathy
- Haemolytic uraemic syndrome (HUS)
- Thrombotic thrombocytopenic purpura (TTP)
- Scleroderma renal crisis
- Medium- and small-vessel vasculitis
- Heavy metal poisoning
- Rhabdomyolysis (myoglobinuria)

# Step-by-step diagnostic approach

Proteinuria is often diagnosed incidentally on routine dipstick testing of urine samples. At other times, an appropriate index of suspicion is required to specifically request urinalysis for protein measurement. It is important to distinguish benign, self-limiting aetiologies from more significant illness. Although the list of differential diagnoses for proteinuria includes almost all aetiologies of kidney disease, it is useful to consider several principles when assessing proteinuria. In general, diseases that affect pre-glomerular structures (e.g., medium-vessel vasculitis, heart failure), macroscopic structural abnormalities (e.g., cystic kidney disease, urinary tract obstruction), lower urinary tract infection, ischaemia, and medication toxicity often result in minimal to low-grade proteinuria. Aetiologies of significant proteinuria typically include glomerular diseases and plasma cell dyscrasias. The presence of haematuria with overt proteinuria suggests glomerulonephritis. Although exceptions do exist, it is helpful to work within this framework.

Proteinuria itself typically has few signs or symptoms. Nephrotic-range proteinuria may, on occasion, result in foamy urine, although normal rates of protein excretion can also produce foam if the urine is highly concentrated. Oedema may be present, and with severe ongoing proteinuria, malnutrition, weight loss, and infection may result. Nephrotic-range proteinuria may result in pleural effusions and ascites, with resultant shortness of breath and abdominal distention.

## Historical factors

Transient proteinuria (from fever, heavy physical exertion, urinary tract infection, urological haemorrhage, orthostatic proteinuria) may present with transient symptoms.

- These include fever, recent strenuous exercise, dysuria, urgency, frequency, foul-smelling/cloudy urine, and/or trauma.

Demographically, age and ethnicity are important historical factors.

Age

- Presentation of proteinuria in children/adolescents is commonly due to orthostatic proteinuria and minimal change disease.
- Minimal change disease and membranous nephropathy are also common in older patients.

Ethnicity

- Focal segmental glomerulosclerosis and hypertensive nephrosclerosis are more common in black people.
- There is a high incidence of IgA nephropathy in Asians.

Symptoms of persistent proteinuria vary according to the cause.

- Swelling may be a symptom of minimal change disease, focal segmental glomerulosclerosis, membranous nephropathy, membranoproliferative glomerulonephritis, IgA nephropathy, systemic lupus erythematosus (SLE), post-infectious glomerulonephritis, amyloidosis, light and heavy chain deposition diseases, fibrillary and immunotactoid glomerulopathy, light chain cast nephropathy, haemolytic uraemic syndrome (HUS), or thrombotic thrombocytopenic purpura (TTP).
- Patients with IgA nephropathy, anti-glomerular basement membrane (anti-GBM) disease (Goodpasture's syndrome), cystic kidney disease, or aristolochic acid nephropathy may describe gross haematuria.
- Pain may be a symptom of cystic kidney disease, urinary tract obstruction, medium- and small-vessel vasculitis, heavy metal poisoning, renal vein thrombosis, and rhabdomyolysis. Patients with Fabry's disease may have a burning sensation of the hands with exercise and heat.
- Altered bowel habit may be a symptom of hypercalciuria (constipation) and HUS (diarrhoea).
- Seizures may be symptoms of TTP and SLE.

- Polyuria may be a symptom of hypercalciuria, Dent's disease, and urinary tract obstruction.
- Ocular symptoms may be present in patients with Fabry's disease, diabetic nephropathy, hypertension, and cystic kidney disease.
- Respiratory symptoms may be associated with medium- and small-vessel vasculitis, IgA nephropathy, and sclerodermal renal crisis.

Past medical history can reveal useful information.

- Lymphoma and stem cell transplant may be associated with minimal change disease.
- HIV, hypertension, diabetes, prior renal injury, and obesity may be associated with focal segmental glomerulosclerosis.
- SLE, hepatitis B, hepatitis C, syphilis, and stem cell transplant may be associated with membranous nephropathy.
- SLE, hepatitis C, post-infectious glomerulonephritis, endocarditis, cryoglobulinaemia, and thrombotic microangiopathy may be associated with membranoproliferative glomerulonephritis.
- Upper respiratory infection, Crohn's disease, or coeliac disease may be associated with IgA nephropathy.
- Autoimmune disease with rash, photosensitivity, oral ulcers, arthritis, serositis, renal disease, neurological changes, and haematological disease may be associated with SLE.
- Recent infection (typically streptococcal, can be staphylococcal) may be associated with post-infectious glomerulonephritis.
- Arthritis, familial Mediterranean fever, multiple myeloma, or monoclonal gammopathy may be associated with amyloidosis.
- Multiple myeloma and monoclonal gammopathy may also be associated with light and heavy chain deposition diseases.
- Multiple myeloma, monoclonal gammopathy, hepatitis C, and lymphoma may be associated with fibrillary and immunotactoid glomerulopathy.
- Rapidly progressive renal failure may be associated with anti-GBM disease (Goodpasture's syndrome).
- Recent nephrotoxic injury such as hypotension, mechanical ventilation, and ischaemia may be associated with acute tubular injury.
- Uveitis from tubulointerstitial nephritis and uveitis syndrome, viral infection, and systemic disease (e.g., sarcoidosis, Sjogren's disease) may be associated with interstitial nephritis.
- Multiple myeloma may be associated with Fanconi syndrome.
- Kidney stones may be associated with hypercalciuria.
- Chronic kidney disease, rickets, and nephrocalcinosis may be associated with Dent's disease.
- Anaemia and chronic kidney disease between the ages of 30 and 50 years may be associated with aristolochic acid nephropathy.
- Benign prostatic hyperplasia, kidney stones, urinary retention, and gynaecological cancer may be associated with urinary tract obstruction.
- Cerebral haemorrhage, stroke, and childhood nephronophthisis may be associated with cystic kidney disease.
- Insulin resistance/diabetes, dyslipidaemia, and obesity may be associated with metabolic syndrome.
- Diabetes and retinopathy is associated with diabetic nephropathy.

- Eye disease, peripheral and coronary arterial disease, congestive heart failure, hypohidrosis, gastrointestinal dysmotility, and renal failure may be associated with Fabry's disease.
- Recent *Escherichia coli* infection, diarrhoea, prior history of HUS/TTP, and prior bone marrow transplant may be associated with HUS/TTP.
- Pregnancy or postnatal state may be associated with HUS.
- Scleroderma is associated with scleroderma renal crisis.
- Multi-organ disorder, neuropathy, headache, cerebrovascular accident, and acute renal failure may be associated with medium- and small-vessel vasculitis.
- Recent crush injury, prolonged immobility, or viral infection may be associated with rhabdomyolysis.

Family history may be positive for the following diseases.

- Atypical HUS/TTP
- Fanconi syndrome
- Dent's disease.

Occupational/social history may be relevant.

- Industrial/environmental exposures to old paint and moonshine are common sources for heavy metal (lead) poisoning.
- Patients with anti-GBM disease (Goodpasture's syndrome) and idiopathic nodular glomerulosclerosis often have positive smoking histories.

Drug history may also reveal important information.

- Non-steroidal anti-inflammatory drugs (NSAIDs), interferon, and lithium may be associated with minimal change disease.
- Bisphosphonates and heroin use may be associated with focal segmental glomerulosclerosis.
- NSAIDs, gold, and penicillamine may be associated with membranous nephropathy.
- NSAIDs, aminoglycosides, amphotericin B, zoledronic acid, oral phosphate bowel preparations, and IV contrast may be associated with acute tubular injury.
- NSAIDs, antibiotics, allopurinol, and proton pump inhibitors may be associated with interstitial nephritis.
- Heavy metal exposure and medications such as tenofovir may be associated with Fanconi syndrome.
- Aristolochic acid and other weight loss medications may be associated with aristolochic acid nephropathy (previously called Chinese herb nephropathy). Aristolochic acid weight loss medications may also be associated with tubulointerstitial disease.
- Ciclosporin, clopidogrel, gemcitabine, and bevacizumab (vascular endothelial growth factor inhibitor) may be associated with HUS or TTP.
- Prednisone may be associated with scleroderma renal crisis.
- Statins and cocaine may be associated with rhabdomyolysis.

## Physical examination

Signs of transient proteinuria (from fever, heavy physical exertion, urinary tract infection, urological haemorrhage, orthostatic proteinuria) are present.

- They may include elevated temperature >38.0°C (100.4°F), flank pain (if pyelonephritis), bladder tenderness on palpation, and/or gross haematuria.
- There are no specific findings for heavy physical exertion or orthostatic proteinuria.

Signs of persistent proteinuria vary according to the cause.

- Fever may be a sign of interstitial nephritis, Fabry's disease, HUS, or TTP.
- Volume overload (in the form of pleural effusion, ascites, or peripheral oedema) may be a sign of minimal change disease, focal segmental glomerulosclerosis, membranous nephropathy, membranoproliferative glomerulonephritis, IgA nephropathy, SLE, post-infectious glomerulonephritis, amyloidosis, light and heavy chain deposition diseases, fibrillary and immunotactoid glomerulopathy, light chain cast nephropathy, HUS, or TTP.
- Hypertension itself may cause proteinuria or may be a sign of other causes, including HUS, TTP, scleroderma renal crisis, glomerular disease, IgA nephropathy, SLE, post-infectious glomerulonephritis, amyloidosis, light and heavy chain deposition disease, fibrillary and immunotactoid glomerulopathy, light chain cast nephropathy, metabolic syndrome, and Fabry's disease.
- Neurological weakness may be a sign of hypercalciuria, heavy metal poisoning, SLE, diabetic neuropathy, or medium- and small-vessel vasculitis.
- Altered mental status may be a sign of hypercalciuria, TTP, medium- and small-vessel vasculitis, heavy metal poisoning, or SLE.
- High BMI may be a sign of metabolic syndrome, Fabry's disease, or focal segmental glomerulosclerosis.
- Rash may be a sign of membranoproliferative glomerulonephritis, cryoglobulinaemia, interstitial nephritis, HUS, TTP, medium- and small-vessel vasculitis, heavy metal poisoning, Fanconi syndrome, or SLE.

DIAGNOSIS

## Who to test

- Patients with chronic kidney disease. In these patients, measurement and treatment of proteinuria is an appropriate healthcare quality performance measure.[3] [39] [40]
- Patients with hypertension require screening for moderately increased albuminuria at diagnosis and then annually in high-risk groups (e.g., diabetes mellitus, reduced kidney function).[41]
- Patients with type 1 diabetes mellitus require annual screening for moderately increased albuminuria at ≥5 years after diagnosis, and patients with type 2 diabetes mellitus require screening at time of diagnosis.[42]
- Patients with metabolic syndrome.
- As part of the assessment of patients with oedema, acute kidney injury, haematuria, or systemic disease (e.g., cirrhosis, HIV infection, vasculitis).
- Routine testing of the general population is not recommended by professional societies.

## How to test

It is important to distinguish persistent and transient proteinuria. The presence of dipstick-positive proteinuria on 2 urine samples separated by 1 to 2 weeks indicates persistent proteinuria and warrants quantification and further assessment.[3] It is important to have a high index of suspicion for persistent proteinuria. For example, although urinary tract infection

is a common cause of transient haematuria and mild (1+) proteinuria, it is important to at least consider more serious aetiologies of these urinary abnormalities whenever they are encountered. Follow-up testing is important if the clinical situation warrants it. If orthostatic proteinuria is suspected, the protein-to-creatinine ratio in a first morning voided urine specimen should be compared with the ratio from a random sample later in the day. The absence of proteinuria in the morning sample and presence in the daytime sample confirms orthostatic proteinuria.

Although qualitative dipstick testing is still widely used, a negative dipstick does not exclude the presence of proteinuria. Screening for moderately increased albuminuria may be more sensitive for the detection of early glomerular disease than measuring total protein excretion, but either method may be used. Semi-quantitative testing (or preferably direct measurement of a spot or 24-hour urine sample) for calculation of a protein-to-creatinine ratio is recommended. Spot urine from a first morning void is preferred, but an untimed urine sample is acceptable. The use of quantitative methods is particularly important when concern for non-albumin proteins (e.g., light chains in multiple myeloma) exists. Although qualitative methods may be used for the initial detection of proteinuria, quantitative methods should be used for confirmation and ongoing follow-up.[3]

Studies have not evaluated the sensitivity and specificity of one-time proteinuria testing for the diagnosis of chronic kidney disease. Intra-individual variability of urinary albumin is high. Reported co-efficients of variance estimates range from 30% to 50%. Up to 37% of people with moderately increased albuminuria and a glomerular filtration rate (GFR) of 60 mL/minute per 1.73 m^2 or greater did not have moderately or severely increased albuminuria on repeated testing 2 months later.[43]

## Further tests

The presence of persistent proteinuria should prompt assessment of kidney function by estimation of GFR from serum creatinine and/or collection of 24-hour urine for creatinine clearance. GFR can be estimated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula or the Modification of Diet in Renal Disease (MDRD) equation. GFR calculators are available online. [National Kidney Foundation: calculators for health care professionals] In patients with a GFR >60 mL/minute/1.73 m^2, the MDRD equation may underestimate true kidney function. For these patients, 24-hour urine collection for measurement of creatinine clearance may be more accurate. In patients with overt proteinuria, renal imaging by ultrasound or a similarly appropriate modality should be obtained. The work-up of proteinuria is similar for glomerular, tubular, and overflow proteinuria. Further laboratory assessment is directed by the results of a comprehensive history and physical examination. Unless the clinical history overwhelmingly supports tubular proteinuria, glomerular proteinuria typically is assessed first. In instances of tubular or overflow proteinuria, these diagnoses are often rendered in the course of routine assessment.

Further testing for albuminuria includes:

- Lipid profile for assessment of metabolic risk factors
- Haemoglobin A1c for assessment of diabetes mellitus
- Clinical assessment and possibly echocardiography for heart failure
- Measurement of blood pressure.

Further testing for overt proteinuria includes:

- Reviewing medication list for potentially offending agents
- Full blood count with differential to screen for haematological disorders
- Urinalysis with microscopic examination to assess for glucosuria, haematuria, and pyuria
- HIV testing if there is clinical suspicion of HIV
- Hepatitis B and C testing if there is clinical suspicion of infection
- Antinuclear antibody if there is clinical suspicion of autoimmune disease such as SLE
- Double-stranded DNA antibody if there is clinical suspicion of SLE

- CH50, C3, and C4 if there is clinical suspicion of SLE, post-infectious glomerulonephritis, cryoglobulinaemia/hepatitis C, or membranoproliferative glomerulonephritis
- Anti-neutrophil cytoplasmic antibody (ANCA) if there is clinical suspicion of ANCA-associated vasculitis
- Serum and urine protein electrophoresis with immunofixation/serum-free light chain measurement if there is clinical suspicion of a plasma cell dyscrasia
- Rheumatoid factor if there is clinical suspicion of cryoglobulinaemia/hepatitis C
- Cryoglobulins if there is clinical suspicion of hepatitis C or cryoglobulinaemic vasculitis
- Anti-glomerular basement membrane (anti-GBM) antibody if there is clinical suspicion of anti-GBM disease (Goodpasture's syndrome).
- Renal biopsy may be required for prognostic and therapeutic decision-making, and to secure a diagnosis if one is not readily apparent from history and serological testing.

Additionally, if predominately tubular proteinuria is suspected from clinical history or initial work-up, the following tests may be of value:

- Heavy metal screening for the assessment of heavy metal poisoning
- Assessment for glucosuria, phosphaturia, and renal tubular acidosis for the assessment of Fanconi syndrome (if all 3 present in the setting of tubular proteinuria)
- Urinary albumin/beta-2-microglobulin ratio of approximately 1:13 (consistent with tubular proteinuria).

The frequency of follow-up protein measurement varies based on the clinical scenario. Formal guidelines recommend yearly measurement in patients with diabetes mellitus and high-risk patients with hypertension. Although specific recommendations do not exist for patients with abnormal renal function, in general, patients are typically reassessed and protein excretion remeasured 3 to 4 times per year. A particular patient may require more or less frequent monitoring depending on their circumstances.

# Differential diagnosis overview

| Common |
| --- |
| Fever |
| Heavy physical exertion |
| Urinary tract infection |
| Urological haemorrhage |
| Orthostatic proteinuria |
| Minimal change disease |
| Focal segmental glomerulosclerosis |
| Membranous nephropathy |
| Membranoproliferative glomerulonephritis |
| IgA nephropathy |
| Systemic lupus erythematosus |
| Post-infectious glomerulonephritis |
| Acute tubular injury |
| Interstitial nephritis |
| Urinary tract obstruction |
| Metabolic syndrome |
| Diabetic nephropathy |
| Hypertension |
| Medium- and small-vessel vasculitis |
| Rhabdomyolysis (myoglobinuria) |

| Uncommon |
| --- |
| Pregnancy |
| Amyloidosis |
| Light and heavy chain deposition diseases |
| Fibrillary and immunotactoid glomerulopathy |
| Anti-glomerular basement membrane (anti-GBM) disease (Goodpasture's syndrome) |
| Fanconi syndrome |
| Cystic kidney disease |
| Hypercalciuria |
| Dent's disease |
| Aristolochic acid nephropathy |
| Light chain cast nephropathy |
| Fabry's disease |
| Haemolytic uraemic syndrome (HUS) |
| Thrombotic thrombocytopenic purpura (TTP) |
| Scleroderma renal crisis |
| Heavy metal poisoning |
| Idiopathic nodular glomerulosclerosis |
| Proliferative glomerulonephritis with monoclonal IgG deposits |
| Polymyositis |
| Renal vein thrombosis |

# Differential diagnosis

## Common

### ◊ Fever

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| fever | elevated temperature >38.0°C (100.4°F) | »**none:** clinical diagnosis | |

### ◊ Heavy physical exertion

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| recent strenuous exercise | no specific findings | »**repeat urinalysis after 2 days' rest:** no proteinuria | |

### ◊ Urinary tract infection

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| dysuria; cloudy, foul-smelling urine; urinary urgency; urinary frequency | flank tenderness (if pyelonephritis); bladder tenderness on palpation | »**urinalysis:** >5-10 white blood cells per high-power field; bacteria visualised<br>»**urine culture:** >100,000 colonies/mL | |

### ◊ Urological haemorrhage

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| recent instrumentation or trauma to urological system | gross haematuria | »**urinalysis:** + blood<br>Often gross haematuria. | »**CT abdomen:** normal or renal/bladder mass<br>»**renal ultrasound:** normal or renal/bladder mass<br>»**cystoscopy:** normal or may reveal bladder source and allows therapeutic intervention |

## Common

### ◊ Orthostatic proteinuria

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| usually children and adolescents | no specific findings | »**split urine collection:** proteinuria during the day and not at night<br>Collect 12-hour urine for proteinuria and creatinine during the day and separate urine collection during the night. | |

### ◊ Minimal change disease

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| most common in children and older people but occurs at all ages; often sudden onset with marked oedema; may be associated with non-steroidal anti-inflammatory drugs (NSAIDs), interferon, lithium, lymphoma, bee stings, stem cell transplant | marked oedema; BP often normal to low | »**urinalysis:** bland sediment, usually nephrotic-range proteinuria | »**renal biopsy:** normal-appearing glomeruli under light microscopy with effacement of podocyte foot processes under electron microscopy |

### ◊ Focal segmental glomerulosclerosis

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| more common in black people and in patients with HIV infection; can be secondary to hypertension, diabetes, prior renal injury, obesity, bisphosphonates, heroin use | oedema; hypertension | »**urinalysis:** may have mild haematuria; subnephrotic- to nephrotic-range proteinuria<br>»**renal biopsy:** glomeruli with focal areas of sclerosis | »**HIV testing:** normal or positive<br>HIV is associated with collapsing focal sclerosis. |

### ◊ Membranous nephropathy

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| more common in older adults; may be associated with non-steroidal anti-inflammatory drugs | oedema; often hypertensive | »**urinalysis:** may have mild haematuria; subnephrotic- to nephrotic-range proteinuria | »**antinuclear antibody:** normal or positive<br>Positive result may indicate SLE. |

## Common

### ◊ Membranous nephropathy

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| (NSAIDs), gold, penicillamine, adenocarcinoma, SLE, hepatitis B, hepatitis C, syphilis, stem cell transplant | | »**renal biopsy:** glomeruli demonstrate increased mesangial matrix with thickened basement membranes; subepithelial immune deposits with occasional mesangial and subepithelial deposits | »**C3/C4:** normal or low<br>Low results are seen in SLE and hepatitis C.<br><br>»**rapid plasma reagin:** normal or positive<br>Positive result may indicate syphilis.<br><br>»**HBsAg:** normal or positive<br>Positive result indicates hepatitis B infection.<br><br>»**hepatitis C Ab:** normal or positive<br>Positive result indicates hepatitis C infection.<br><br>»**age-appropriate cancer screening:** normal or malignancy<br>Malignancy, especially adenocarcinoma is associated with membranous nephropathy. |

### ◊ Membranoproliferative glomerulonephritis

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| idiopathic is rare; generally hx of another disease such as SLE, hepatitis C, post-infectious glomerulonephritis, endocarditis, cryoglobulinaemia, thrombotic microangiopathy | oedema; often hypertensive; may have evidence of arthritis/rash/other end-organ involvement with SLE; murmur with endocarditis; tea-coloured urine with post-infectious glomerulonephritis | »**urinalysis:** often with haematuria, may have red blood cell casts; subnephrotic- to nephrotic-range proteinuria<br><br>»**renal biopsy:** glomeruli demonstrate lobulated tufts with increased mesangial matrix, endothelial cell proliferation, and thickened basement membranes; subendothelial and mesangial deposits | »**antinuclear antibody:** normal or positive<br>Positive result may indicate SLE.<br><br>»**hepatitis C Ab:** normal or positive<br>Membranoproliferative glomerulonephritis is associated with chronic viral hepatitis.<br><br>»**C3/C4:** normal or low<br>Low results are seen in SLE and hepatitis C. |

## Common

### ◊ Membranoproliferative glomerulonephritis

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| | | | »**cryoglobulins:** normal or positive<br>Positive result is associated with cryoglobulinaemic vasculitis, hepatitis C, and plasma cell dyscrasia.<br><br>»**rheumatoid factor:** normal or positive<br>Positive result may indicate presence of cryoglobulins.<br><br>»**full blood count:** schistocytes and thrombocytopenia in thrombotic microangiopathy |

### ◊ IgA nephropathy

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| most common glomerulonephritis worldwide; high incidence in Asians; hx of gross haematuria associated with upper respiratory infection; hx of Crohn's disease or coeliac disease | may or may not have oedema and hypertension; often discovered incidentally while assessing microscopic haematuria | »**urinalysis:** typically subnephrotic-range proteinuria<br><br>»**renal biopsy:** glomeruli range from mild increase in mesangial matrix to crescent glomerulonephritis; mesangial deposits that stain for IgA | »**liver function tests:** normal or abnormal<br>Cirrhosis can cause a secondary IgA nephropathy.<br><br>»**oesophagogastroduodenoscopy/colonoscopy:**<br>Crohn's disease: aphthous ulcers, hyperaemia, oedema, cobblestoning, skip lesions; coeliac sprue: villous atrophy, mucosal fissuring, and nodularity<br>Should be pursued if clinically indicated. Crohn's disease and coeliac sprue are associated with IgA nephropathy. |

DIAGNOSIS

## Common

### ◊ Systemic lupus erythematosus

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| hx of rash, photosensitivity, oral ulcers, arthritis, serositis, renal disease, neurological changes (psychosis, seizures), haematological disease | malar rash; arthritis; oedema; hypertension; oral ulcers; pleural effusion; neuropathy; Raynaud's phenomena | »**urinalysis:** may have haematuria, red blood cell casts, and pyuria; subnephrotic- to nephrotic-range proteinuria<br>»**renal biopsy:** biopsy findings range from mild mesangial proliferation to crescentic glomerulonephritis; may also result in a membranous nephropathy or interstitial nephritis<br>»**antinuclear antibody:** positive | »**double-stranded DNA/anti-Smith:** normal or positive<br>Positive result is more common with renal disease.<br>»**C3/C4:** normal or low<br>Often decreased. |

### ◊ Post-infectious glomerulonephritis

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| recent hx of infection; can occur with virtually any infectious agent; classic description is post-streptococcal; *Staphylococcus aureus* super-antigens can result in rapid acute kidney injury | oedema; hypertension; tea-coloured urine in some cases | »**urinalysis:** haematuria and red blood cell casts; typically subnephrotic-range proteinuria<br>»**renal biopsy:** glomeruli have large subepithelial hump-like deposits; crescents and endocapillary proliferation are common, and glomeruli may have a membranoproliferative appearance | »**antistreptolysin O (ASO) titre :** normal or elevated<br>ASO titre is elevated post-streptococcal infection but does not exclude non-streptococcal-associated post-infectious glomerulonephritis.<br>»**C3/C4:** normal or low<br>Often decreased with post-infectious glomerulonephritis. |

### ◊ Acute tubular injury

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| recent nephrotoxic injury such as hypotension, | no specific findings | »**urinalysis:** typically acellular with granular | »**renal biopsy:** proximal tubular injury, loss of brush border, vacuolisation of tubular epithelial cells |

## Common

### ◊ Acute tubular injury

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| non-steroidal anti-inflammatory drugs (NSAIDs), aminoglycosides, amphotericin B, zoledronic acid, oral phosphate bowel preparations, IV contrast, mechanical ventilation, ischaemia | | muddy-brown casts; minimal proteinuria; renal tubular epithelial (RTE) cells, RTE casts, waxy casts | Definitive but generally not required. [Fig-6] [Fig-7] |

### ◊ Interstitial nephritis

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| exposure to typical offending medications such as non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics, allopurinol, proton pump inhibitors; uveitis in the tubulointerstitial nephritis and uveitis syndrome; infectious agents (e.g., viruses); systemic disease (e.g., sarcoidosis, Sjogren's disease) | may have rash and fever; anterior uveitis in tubulointerstitial nephritis and uveitis syndrome | »**urinalysis:** pyuria; white blood cell cast; may have haematuria; subnephrotic-range proteinuria<br>»**full blood count:** eosinophilia<br>Eosinophilia is present <50% of the time. | »**renal biopsy:** interstitial nephritis with eosinophils<br>Definitive but generally not required unless renal function does not improve after stopping offending medication. |

### ◊ Urinary tract obstruction

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| hx of benign prostatic hyperplasia, kidney stones, urinary retention, gynaecological cancer; may have decreased, normal, or increased urine output; flank or suprapubic pain | palpable bladder may be present; enlarged prostate on rectal examination | »**urinalysis:** typically acellular; minimal proteinuria<br>Typically acellular unless there is a mass invading the ureters/bladder.<br>»**renal ultrasound:** distended bladder with benign prostatic hyperplasia; hydronephrosis/hydroureter with ureteral obstruction | »**Foley catheter:** large urine output if bladder outlet is obstructed<br>Placement of a Foley helps confirm/reject bladder outlet obstruction.<br>»**computed tomography abdomen:** hydronephrosis<br>Useful but more expensive and uses ionising radiation as compared with ultrasound. |

## Common

### ◊ Metabolic syndrome

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| overweight; hx of hypertension, insulin resistance/diabetes, dyslipidaemia | BP ≥130/85 mmHg; waist ≥102 cm (40 inches) in men or 89 cm (35 inches) in women | »**lipid profile:** triglyceride ≥1.7 mmol/L (≥150 mg/dL); high-density lipoprotein <1.03 mmol/L (<40 mg/dL) in men or <1.3 mmol/L (<50 mg/dL) in women<br>»**fasting blood sugar:** ≥5.5 mmol/L (≥100 mg/dL) | |

### ◊ Diabetic nephropathy

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| increases with duration of diabetes; retinopathy is typically present | retinopathy; neuropathy; often hypertensive with macrovascular complications | »**urinalysis:** usually >1 g/day proteinuria<br>Often in the nephrotic range.<br>»**renal biopsy:** increased mesangial matrix with Kimmelstiel-Wilson nodules | |

### ◊ Hypertension

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| long-standing hx of hypertension | evidence of hypertensive end-organ damage (e.g., retinopathy, left ventricular hypertrophy) | »**urinalysis:** usually subnephrotic-range proteinuria<br>»**renal biopsy:** evidence of hypertensive vascular changes and nephrosclerosis | »**echocardiogram:** normal or left ventricular hypertrophy<br>Most patients have evidence of other end-organ involvement, although not specific for hypertensive nephropathy. |

### ◊ Medium- and small-vessel vasculitis

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| multi-organ disorder; rash, neuropathy, headache, | specific organ involvement dictates findings; typically | »**urinalysis:** medium-vessel vasculitis: | »**cytoplasmic anti-neutrophil** |

DIAGNOSIS

## Common

### ◊ Medium- and small-vessel vasculitis

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| cerebrovascular accident, change in mental status, shortness of breath, haemoptysis, abdominal pain, acute renal failure | multiple systems are involved simultaneously | typically acellular and minimal proteinuria; small-vessel vasculitis: haematuria, red blood cell casts, and usually subnephrotic-range proteinuria<br>»**renal biopsy:** small-vessel vasculitis produces a crescentic glomerulonephritis without significant endothelial proliferation or marked immune complex deposition<br>»**angiography:** normal or polyarteritis nodosa (PAN) PAN can be diagnosed by renal angiogram. | **cytoplasmic antibody:** normal or positive Usually positive with Wegener's vasculitis. Usually negative in PAN.<br>»**perinuclear anti-neutrophil cytoplasmic antibody:** normal or positive Usually positive with microscopic polyangiitis and Churg-Strauss syndrome. |

### ◊ Rhabdomyolysis (myoglobinuria)

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| muscle pain; recent crush injury; prolonged immobility; viral infection; use of drugs such as statins and cocaine; inborn errors of muscle metabolism may present in young adults | muscle tenderness; dark urine | »**urinalysis:** haem pigments without red blood cells; subnephrotic-range proteinuria<br>»**creatine kinase:** usually >5000 to 10,000 U/L | »**urine myoglobin:** normal or positive Positive assay indicates presence of urine myoglobin. Assay is insensitive and typically adds little to the assessment. |

## Uncommon

### ◊ Pregnancy

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| worsening of pre-existing chronic kidney disease; development of new-onset hypertension and/or oedema during pregnancy (e.g., pre-eclampsia); | hypertension; oedema; bruising/petechiae (with TTP-HUS) | »**urinalysis:** subnephrotic- to nephrotic-range proteinuria; bland sediment with pre-eclampsia; may have haematuria in TTP-HUS | »**renal biopsy:** glomerular endotheliosis in pre-eclampsia; glomerular thrombosis can be seen, although renal biopsy is |

## Uncommon

### ◊ Pregnancy

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| possible thrombotic thrombocytopenic purpura (TTP)-haemolytic uraemic syndrome (HUS) | | »**uric acid:** usually >357 micromol/L (6 mg/dL) in pre-eclampsia<br>»**urea and creatinine:** may be elevated<br>»**peripheral blood smear:** schistocytes; anaemia; thrombocytopenia if TTP-HUS | often not obtained due to thrombocytopenia |

### ◊ Amyloidosis

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| chronic inflammatory diseases such as rheumatoid arthritis, restrictive heart disease, liver failure, and familial Mediterranean fever; plasma cell dyscrasia such as multiple myeloma or monoclonal gammopathy of undetermined significance | oedema; hypertension; may have carpal tunnel syndrome; capillary fragility; autonomic insufficiency | »**urinalysis:** haematuria; subnephrotic- to nephrotic-range proteinuria<br>»**renal biopsy:** glomerular amyloid deposits Amyloid demonstrates apple-green birefringence under polarised light; fibrils typically 8 to 12 nanometres in diameter on electron microscopy.<br>»**protein electrophoresis:** a monoclonal protein is typically evident on serum and urine electrophoresis | »**bone marrow biopsy:** may reveal evidence of plasma cell dyscrasia Congo red stain is used. [Fig-3] |

## Uncommon

### ◊ Light and heavy chain deposition diseases

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| plasma cell dyscrasia such as multiple myeloma or monoclonal gammopathy of undetermined significance | oedema; hypertension; autonomic insufficiency | »**urinalysis:** may have haematuria and subnephrotic- to nephrotic-range proteinuria<br>»**renal biopsy:** glomerular and tubular deposits of light chains<br>Deposits are typically granular-powdery under electron microscopy.<br>»**protein electrophoresis:** monoclonal protein, elevated kappa or lamda light chain levels<br>Typically evident on serum and urine electrophoresis. | »**bone marrow biopsy:** normal or plasma cell dyscrasia<br>Shows results of multiple myeloma. [Fig-4] [Fig-5] |

### ◊ Fibrillary and immunotactoid glomerulopathy

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| plasma cell dyscrasia such as multiple myeloma or monoclonal gammopathy; hepatitis C; some patients have underlying lymphoma | oedema; hypertension | »**urinalysis:** haematuria; subnephrotic- to nephrotic-range proteinuria<br>»**renal biopsy:** deposits of fibrils visualised by electron microscopy<br>Fibrillary fibrils typically 18 to 22 nanometres in diameter and randomly arranged; immunotactoid typically 30 to 90 nanometres with microtubular structure.<br>»**protein electrophoresis:** normal or monoclonal protein<br>Immunotactoid is associated with monoclonal gammopathy of undetermined significance and underlying plasma cell dyscrasia. | |

## Uncommon

### ◊ Anti-glomerular basement membrane (anti-GBM) disease (Goodpasture's syndrome)

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| rapidly progressive renal failure, haemoptysis, haematuria; often has positive smoking hx | crackles; may have gross haematuria | »**urinalysis:** haematuria; proteinuria typically minimal to <2 g/day<br>»**anti-GBM antibody:** positive (≥3 U/mL)<br>»**chest x-ray:** pulmonary haemorrhage<br>»**renal biopsy:** crescentic, non-proliferative glomerulonephritis; linear IgG glomerular basement membrane staining | |

### ◊ Fanconi syndrome

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| can be inherited; may have underlying multiple myeloma, heavy metal exposure, or medications such as tenofovir | microcephaly, hypogonadism, and café au lait spots with congenital disease; adult-onset symptoms specific to underlying aetiology | »**urinalysis:** low-molecular-weight proteinuria/subnephrotic-range proteinuria; glycosuria; proximal renal tubular acidosis; phosphaturia<br>»**serum electrolytes:** hypophosphataemia; hypokalaemia; non-anion gap acidosis | »**leukocyte chromosomal breakage assay:** increased breakage in congenital Fanconi anaemia relative to controls<br>Can diagnose congenital Fanconi anaemia.<br>»**protein electrophoresis:** monoclonal protein<br>May reveal evidence of plasma cell dyscrasia and associated light chain disease. |

### ◊ Cystic kidney disease

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| chronic kidney disease in childhood with nephronophthisis; may have flank pain or haematuria with polycystic kidney disease (PKD); cerebral | palpable kidneys in PKD; retinitis pigmentosa in some forms of nephronophthisis; polydactyly in Bardet-Biedl syndrome | »**urinalysis:** usually acellular; minimal proteinuria<br>»**ultrasound:** small cystic kidneys with nephronophthisis; | |

## Uncommon

### ◊ Cystic kidney disease

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| haemorrhage/stroke in PKD | | enlarged cystic kidneys with PKD | |

### ◊ Hypercalciuria

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| usually asymptomatic; may have hx of kidney stones; if also hypercalcaemic, may have nausea, constipation, psychosis, polyuria, weakness | if hypercalcaemic, may have change in mental status, generalised weakness | »**urinalysis:** may have haematuria; subnephrotic-range proteinuria<br>Haematuria detected in cases of kidney stones.<br><br>»**urine calcium excretion:** >300 mg in men and >250 mg in women | »**renal ultrasound:** may reveal evidence of nephrocalcinosis |

### ◊ Dent's disease

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| X-linked recessive: typically only males are affected; polyuria and nocturia in childhood; kidney stones; chronic kidney disease; rickets; nephrocalcinosis | few physical findings | »**urinalysis:** low molecular weight/subnephrotic range proteinuria; may have haematuria; hypercalciuria; glycosuria<br>Haematuria detected in cases of kidney stones. | »**CLC-5 gene testing:** gene mutation<br>Available through specialised laboratories. |

### ◊ Aristolochic acid nephropathy

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| has been associated with aristolochic acid ingestion, which is a component of some Chinese herbs and weight loss medications and is a part of wheat used for bread in the Balkan region | few physical findings; may have gross haematuria with underlying urological malignancy | »**urinalysis:** may have mild haematuria and pyuria; proteinuria generally <2 g<br><br>»**renal biopsy:** severe cortical interstitial fibrosis with glomerular sparing; general absence of inflammatory infiltrate | |

## Uncommon

### ◊ Light chain cast nephropathy

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| plasma cell dyscrasia, such as multiple myeloma or monoclonal gammopathy of undetermined significance; rapid onset of renal failure | oedema; hypertension | »**urinalysis:** typically acellular; nephrotic-range proteinuria<br>»**renal biopsy:** light chain casts within the renal tubules without evidence of glomerular deposition or amyloid<br>»**protein electrophoresis:** a monoclonal protein is typically evident on serum and urine electrophoresis | »**bone marrow biopsy:** may reveal evidence of plasma cell dyscrasia Shows results of multiple myeloma. [Fig-4] [Fig-5] |

### ◊ Fabry's disease

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| X-linked genetic deficiency of alpha-galactosidase-A; burning sensation of the hands with exercise and heat, eye disease, peripheral and coronary arterial disease, congestive heart failure, hypohidrosis, gastrointestinal dysmotility, renal failure, and fever | corneal clouding; hypertension; poor circulation; angina; angiokeratomas; hypohidrosis; obesity; telangiectasia; angiokeratomas; corneal deposits | »**urinalysis:** subnephrotic- to nephrotic-range proteinuria<br>»**leukocyte alpha-galactosidase A level:** <4% of normal | »**skin biopsy:** accumulation of glycolipid<br>»**renal biopsy:** accumulation of glycolipid and foam cells Often not required. |

### ◊ Haemolytic uraemic syndrome (HUS)

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| recent *Escherichia coli* infection; diarrhoea; in cases of atypical HUS, there is prior hx of HUS/thrombotic thrombocytopenic purpura; positive FHx; hx of complement regulatory protein mutations; prior bone marrow transplant; associated with | oedema; hypertension; petechial rash or purpura; fever | »**urinalysis:** may be acellular or with haematuria; proteinuria typically minimal to <2 g/day<br>»**full blood count:** low Hb and platelets<br>»**peripheral blood smear:** schistocytes, thrombocytopenia<br>»**haptoglobin:** normal or low | »**stool culture on sorbitol-MacConkey agar to detect E coli O157:H7 or O104:H4:** translucent colonies (these can be further investigated with antisera to the antigens)<br>»**renal biopsy:** glomerular thrombosis can be seen, although renal biopsy is often not obtained due to thrombocytopenia |

## Uncommon

### ◊ Haemolytic uraemic syndrome (HUS)

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| medications such as ciclosporin, gemcitabine, and bevacizumab (vascular endothelial growth factor inhibitor); pregnancy or postnatal state | | Decreased in presence of systemic haemolysis.<br>»**urea and creatinine:** elevated<br>Associated with acute renal failure.<br>»**lactate dehydrogenase:** normal or elevated<br>May indicate haemolysis if elevated.<br>»**ADAMTS13 activity:** usually normal | »**complement mutation analysis:** may detect mutations in ≥1 members of complement pathway |

### ◊ Thrombotic thrombocytopenic purpura (TTP)

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| recent infection; mental status changes ranging from headache and confusion to seizures; prior hx of TTP; positive FHx; prior bone marrow transplant; associated with medications such as ciclosporin, clopidogrel, and gemcitabine | oedema; hypertension, petechial rash or purpura; fever; focal neurological deficits, and coma | »**urinalysis:** may be acellular or with haematuria; proteinuria typically minimal to <2 g/day<br>»**full blood count:** low Hb and platelets<br>»**peripheral blood smear:** schistocytes, thrombocytopenia<br>»**haptoglobin:** normal or low<br>Decreased in presence of systemic haemolysis.<br>»**urea and creatinine:** elevated<br>Associated with acute renal failure.<br>»**lactate dehydrogenase:** normal or elevated<br>May indicate haemolysis if elevated.<br>»**ADAMTS13 activity:** low | »**renal biopsy:** glomerular thrombosis can be seen, although renal biopsy is often not obtained due to thrombocytopenia |

## Uncommon

### ◊ Scleroderma renal crisis

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| usually within first 5 years of scleroderma diagnosis with diffuse skin involvement; patients often taking prednisone; new-onset hypertension and rapidly worsening renal function; may have gastrointestinal dysmotility and pulmonary hypertension | often marked hypertension (often abrupt onset); masked facies of scleroderma; tapered digits with tight skin | »**creatinine:** rapidly rising<br>»**urinalysis:** may be acellular or with mild haematuria; proteinuria typically minimal to <2 g/day<br>Bland urine sediment in absence of alternative aetiology. | »**renal biopsy:** demonstrates onion-skinned vascular lesions; may have evidence of thrombotic microangiopathy |

### ◊ Heavy metal poisoning

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| hx of industrial/environmental exposure; old paint and moonshine are common sources for lead poisoning; may have neuropathy, hypertension, abdominal pain, psychiatric symptoms, gout, rash | gout, neuropathy, developmental delay, hyperkeratosis, hypertension | »**urinalysis:** often acellular; subnephrotic-range proteinuria<br>»**urine heavy metal testing:** positive | »**renal biopsy:** non-specific findings of interstitial fibrosis |

### ◊ Idiopathic nodular glomerulosclerosis

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| hx of smoking and obesity | obesity, oedema | »**urinalysis:** acellular, nephrotic-range proteinuria | »**renal biopsy:** nodular glomerulosclerosis |

### ◊ Proliferative glomerulonephritis with monoclonal IgG deposits

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| hx of monoclonal gammopathy | oedema | »**urinalysis:** subnephrotic-range proteinuria with haematuria<br>»**serum:** monoclonal spike | »**renal biopsy:** granular non-organised deposits on electron microscopy |

## Uncommon

### ◊ Polymyositis

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| hx of muscle pain and weakness | muscle weakness | »**urinalysis:** subnephrotic-range proteinuria<br>»**serum:** anti-synthetase antibodies (anti-Jo1), elevated CK | »**MRI:** muscle oedema and inflammation<br>»**muscle biopsy:** cellular infiltrate with the fascicle |

### ◊ Renal vein thrombosis

| History | Exam | 1st Test | Other tests |
|---|---|---|---|
| most common in patients with nephrotic syndrome (primarily membranous nephropathy), antiphospholipid antibody syndrome, and other inherited prothrombotic defects; extrinsic compression of the renal vein by retroperitoneal fibrosis or aortic aneurysm; hx of trauma or severe dehydration; in children presents with acute flank pain | haematuria, oedema | »**urinalysis:** haematuria; subnephrotic- to nephrotic-range proteinuria<br>»**urea and creatinine:** elevated if bilateral or unilateral thrombosis is present in the setting of chronic kidney disease<br>»**LDH:** may be elevated | »**selective renal venography:** shows renal vein occlusion<br>»**MRI, CT, or Doppler ultrasound:** shows renal vein occlusion |

DIAGNOSIS

# Diagnostic guidelines

## International

### KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease

**Published by:** Kidney Disease: Improving Global Outcomes
**Last published:** 2012

## North America

### Screening for chronic kidney disease: US Preventive Services Task Force recommendation statement

**Published by:** US Preventive Services Task Force
**Last published:** 2012

## Oceania

### Chronic kidney disease and measurement of albuminuria or proteinuria: a position statement

**Published by:** Australasian Proteinuria Consensus Working Group
**Last published:** 2012

# Online resources

1. National Kidney Foundation: calculators for health care professionals *(external link)*

## Key articles


- National Kidney Foundation. KDOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002;39(suppl 1):S1-S266. Full text Abstract
- Wright JT Jr, Bakris G, Greene T, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. JAMA. 2002;288:2421-2431. Full text Abstract
- Kidney Disease: Improving Global Outcomes. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. January 2013. http://www.kdigo.org (last accessed 28 June 2016). Full text
- Ginsberg JM, Chang BS, Matarese RA, et al. Use of single voided urine samples to estimate quantitative proteinuria. N Engl J Med. 1983;309:1543-1546. Abstract


## References


1. Viswanathan G, Upadhyay A. Assessment of proteinuria. Adv Chronic Kidney Dis. 2011;18:243-248. Abstract
2. Montañés Bermúdez R, Gràcia García S, Pérez Surribas D, et al. Consensus document. Recommendations on assessing proteinuria during the diagnosis and follow-up of chronic kidney disease. Nefrologia. 2011;31:331-345. Abstract
3. National Kidney Foundation. KDOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002;39(suppl 1):S1-S266. Full text Abstract
4. Levey AS, de Jong PE, Coresh J, et al. The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report. Kidney Int. 2011;80:17-28. Abstract
5. Chronic Kidney Disease Prognosis Consortium; Matsushita K, van der Velde M, Astor BC, et al. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. Lancet. 2010;375:2073-2081. Abstract
6. Astor BC, Matsushita K, Gansevoort RT, et al. Lower estimated glomerular filtration rate and higher albuminuria are associated with mortality and end-stage renal disease. A collaborative meta-analysis of kidney disease population cohorts. Kidney Int. 2011;79:1331-1340. Abstract
7. van der Velde M, Matsushita K, Coresh J, et al. Lower estimated glomerular filtration rate and higher albuminuria are associated with all-cause and cardiovascular mortality. A collaborative meta-analysis of high-risk population cohorts. Kidney Int. 2011;79:1341-1352. Abstract
8. Gansevoort RT, Matsushita K, van der Velde M, et al. Lower estimated GFR and higher albuminuria are associated with adverse kidney outcomes. A collaborative meta-analysis of general and high-risk population cohorts. Kidney Int. 2011;80:93-104. Abstract
9. British Medical Journal. Low eGFR and high albuminuria predict end stage kidney disease and death at all ages. BMJ. 2012;345:e7478. Abstract
10. Han SS, Ahn SY, Ryu J, et al. Proteinuria and hematuria are associated with acute kidney injury and mortality in critically ill patients: a retrospective observational study. BMC Nephrol. 2014;15:93. Full text Abstract
11. Lin LY, Jenq CC, Liu CS, et al. Proteinuria can predict short-term prognosis in critically ill cirrhotic patients. J Clin Gastroenterol. 2014;48:377-382. Abstract

REFERENCES


12. Borrego J, Mazuecos A, Gentil MA, et al. Proteinuria as a predictive factor in the evolution of kidney transplantation. Transplant Proc. 2013;45:3627-3629. Abstract

13. Lewis EJ, Hunsicker LG, Bain RP, et al. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. N Engl J Med. 1993;329:1456-1462. Full text Abstract

14. The GISEN Group. Randomised placebo-controlled trial of effect of ramipril on decline in glomerular filtration rate and risk of terminal renal failure in proteinuric, non-diabetic nephropathy. Lancet. 1997;349:1857-1863. Abstract

15. Brenner BM, Cooper ME, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med. 2001;345:861-869. Full text Abstract

16. Lewis EJ, Hunsicker LG, Clarke WR, et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med. 2001;345:851-860. Full text Abstract

17. Parving HH, Lehnert H, Bröchner-Mortensen J, et al; Irbesartan in Patients with Type 2 Diabetes and Microalbuminuria Study Group. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. N Engl J Med. 2001;345:870-878. Full text Abstract

18. Wright JT Jr, Bakris G, Greene T, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. JAMA. 2002;288:2421-2431. Full text Abstract

19. Inker LA, Levey AS, Pandya K, et al. Early change in proteinuria as a surrogate end point for kidney disease progression: an individual patient meta-analysis. Am J Kidney Dis. 2014;64:74-85. Abstract

20. Kidney Disease: Improving Global Outcomes. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. January 2013. http://www.kdigo.org (last accessed 28 June 2016). Full text

21. Grams ME, Li L, Greene TH, et al. Estimating time to ESRD using kidney failure risk equations: results from the African American Study of Kidney Disease and Hypertension (AASK). Am J Kidney Dis. 2015;65:394-402. Abstract

22. Astor BC, Hallan SI, Miller ER 3rd, et al. Glomerular filtration rate, albuminuria, and risk of cardiovascular and all-cause mortality in the US population. Am J Epidemiol. 2008;167:1226-1234. Full text Abstract

23. Kawar B, Bello AK, El Nahas AM. High prevalence of microalbuminuria in the overweight and obese population: data from a UK population screening programme. Nephron Clin Pract. 2009;112:c205-c212. Abstract

24. Siedner MJ, Gelber AC, Rovin BH, et al. Diagnostic accuracy study of urine dipstick in relation to 24-hour measurement as a screening tool for proteinuria in lupus nephritis. J Rheumatol. 2008;35:84-90. Abstract

25. White SL, Yu R, Craig JC, et al. Diagnostic accuracy of urine dipsticks for detection of albuminuria in the general community. Am J Kidney Dis. 2011;58:19-28. Abstract

26. Comper WD, Osicka TM. Detection of urinary albumin. Adv Chronic Kidney Dis. 2005;12:170-176. Abstract

27. McTaggart MP, Newall RG, Hirst JA, et al. Diagnostic accuracy of point-of-care tests for detecting albuminuria: a systematic review and meta-analysis. Ann Intern Med. 2014;160:550-557. Abstract

28. Wu HY, Peng YS, Chiang CK, et al. Diagnostic performance of random urine samples using albumin concentration vs ratio of albumin to creatinine for microalbuminuria screening in patients with diabetes mellitus: a systematic review and meta-analysis. JAMA Intern Med. 2014;174:1108-1115. Abstract

29. Ginsberg JM, Chang BS, Matarese RA, et al. Use of single voided urine samples to estimate quantitative proteinuria. N Engl J Med. 1983;309:1543-1546. Abstract

30. National Institute for Health and Care Excellence. Chronic kidney disease in adults: assessment and management. January 2015. https://www.nice.org.uk/ (last accessed 28 June 2016). Full text

31. Johnson DW, Jones GR, Mathew TH, et al. Chronic kidney disease and measurement of albuminuria or proteinuria: a position statement. Med J Aust. 2012;197:224-225. Full text Abstract

32. Papanna R, Mann LK, Kouides RW, et al. Protein/creatinine ratio in preeclampsia: a systematic review. Obstet Gynecol. 2008;112:135-144. Abstract

33. Côté AM, Brown MA, Lam E, et al. Diagnostic accuracy of urinary spot protein:creatinine ratio for proteinuria in hypertensive pregnant women: systematic review. BMJ. 2008 ;336:1003-1006. Full text Abstract

34. Springberg PD, Garrett LE Jr, Thompson AL Jr, et al. Fixed and reproducible orthostatic proteinuria: results of a 20-year follow up study. Ann Intern Med. 1982;97:516-519. Abstract

35. Hogg RJ, Portman RJ, Milliner D, et al. Evaluation and management of proteinuria and nephrotic syndrome in children: recommendations from a pediatric nephrology panel established at the National Kidney Foundation conference on proteinuria, albuminuria, risk assessment, detection, and elimination (PARADE). Pediatrics. 2000; 105:1242-1249. Abstract

36. Peterson PA, Evrin PE, Berggard I. Differentiation of glomerular, tubular, and normal proteinuria: determinations of urinary excretion of beta-2-macroglobulin, albumin, and total protein. J Clin Invest. 1969;48:1189-1198. Full text Abstract

37. Kim HH, Kim JY, Kim SJ, et al. Overflow proteinuria as a manifestation of unrecognized polymyositis. Int Med Case Rep J. 2014;7:71-74. Full text Abstract

38. Singhal R, Brimble KS, Thromboembolic complications in the nephrotic syndrome: pathophysiology and clinical management. Thromb Res. 2006;118:397-407. Abstract

39. Keane WF, Eknoyan G. Proteinuria, albuminuria, risk, assessment, detection, elimination (PARADE): a position paper of the National Kidney Foundation. Am J Kidney Dis. 1999;33:1004-1010. Abstract

40. Thorp ML, Smith DH, Johnson ES, et al. Proteinuria among patients with chronic kidney disease: a performance measure for improving patient outcomes. Jt Comm J Qual Patient Saf. 2012;38:277-282. Abstract

41. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003;42:1206-1252. Full text Abstract

42. American Diabetes Association. Standards of medical care in diabetes - 2010. Diabetes Care. 2010;33(suppl 1):S11-S61. Full text Abstract

43. Moyer VA; U.S. Preventive Services Task Force. Screening for chronic kidney disease: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2012;157:567-570. Full text Abstract

# Images



| | Urine albumin | Urine total protein | Serum albumin | Detail |
|---|---|---|---|---|
| **Microalbuminuria** | 20-200 mg/g creatinine (men); 30-300 mg/g creatinine (women) | | | Associated with increased risk of progressive kidney disease and future cardiovascular events in many populations. |
| **Overt albuminuria** | >300 mg/day | | | |
| **Overt proteinuria** | | ≥300 mg/day | | In many renal diseases, larger amounts of proteinuria are associated with worse renal survival. |
| **Nephrotic range proteinuria** | | ≥3.5 g/day | <3.0 g/dL | The presence of nephrotic-range proteinuria with oedema, hypoalbuminaemia, and hyperlipidaemia is defined as nephrotic syndrome. |
| **Glomerular proteinuria** | 1-20 g/day | | | Passage of protein from glomerular capillary blood (mainly albumin) into the urine. |
| **Tubular proteinuria** | | <2 g/day | | Passage of low-molecular-weight proteins (e.g., retinol-binding protein, alpha-2-microglobulin, beta-2-microglobulin) into the urine. |
| **Overflow proteinuria** | | up to 20 g/day | | Overproduction of small proteins (e.g., myoglobin, light chains) leads to increased glomerular filtration and appearance in the urine. |

*Figure 1: Proteinuria definitions*

*Created by authors*

| | |
|---|---|
| negative | 0 mg/dL |
| trace | 15-30 mg/dL |
| 1+ | 30-100 mg/dL |
| 2+ | 100-300 mg/dL |
| 3+ | 300-1000 mg/dL |
| 4+ | >1000 mg/dL |

*Figure 2: Dipstick proteinuria ranges*

*Created by BMJ Evidence Centre using author content*



IMAGES

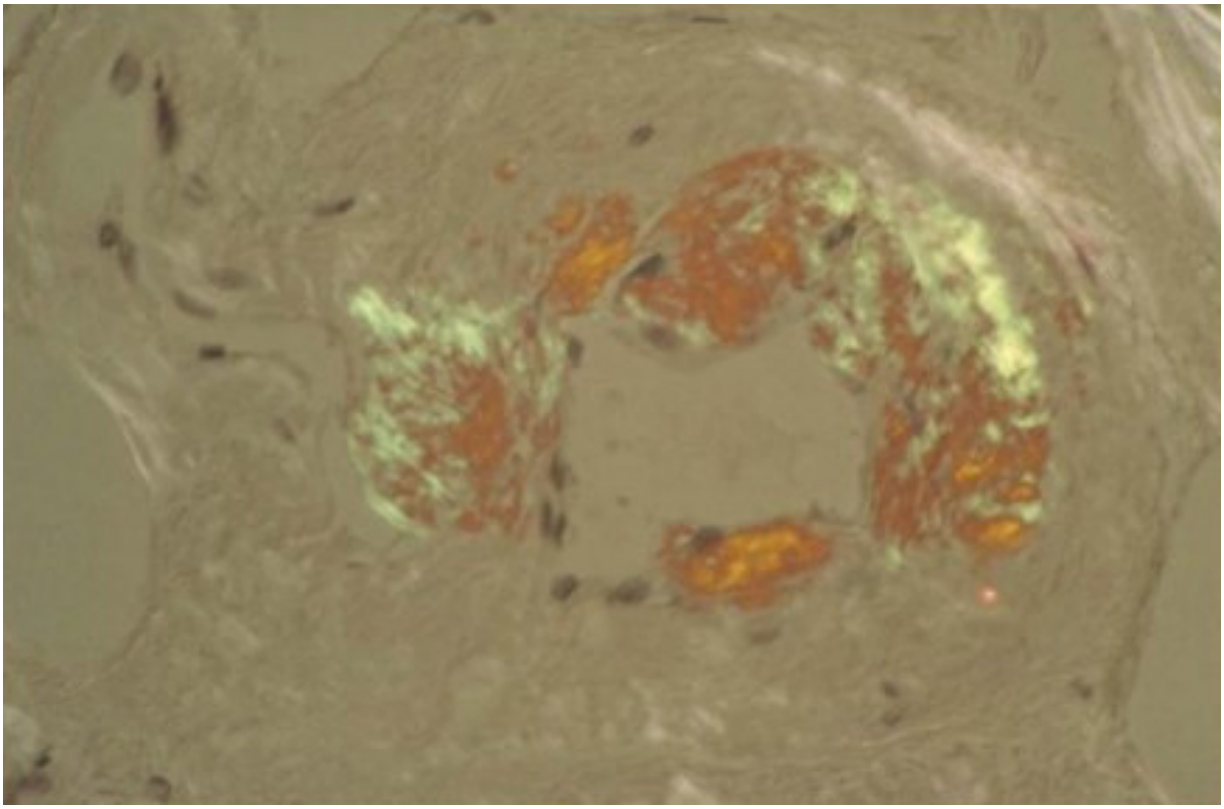


*Figure 3: Amyloidosis: Congo red stained blood vessel in a bone marrow biopsy demonstrating pathognomonic green birefringence*

*Courtesy of Dr Morie A. Gertz, Hematology, Mayo Clinic, Rochester, MN*

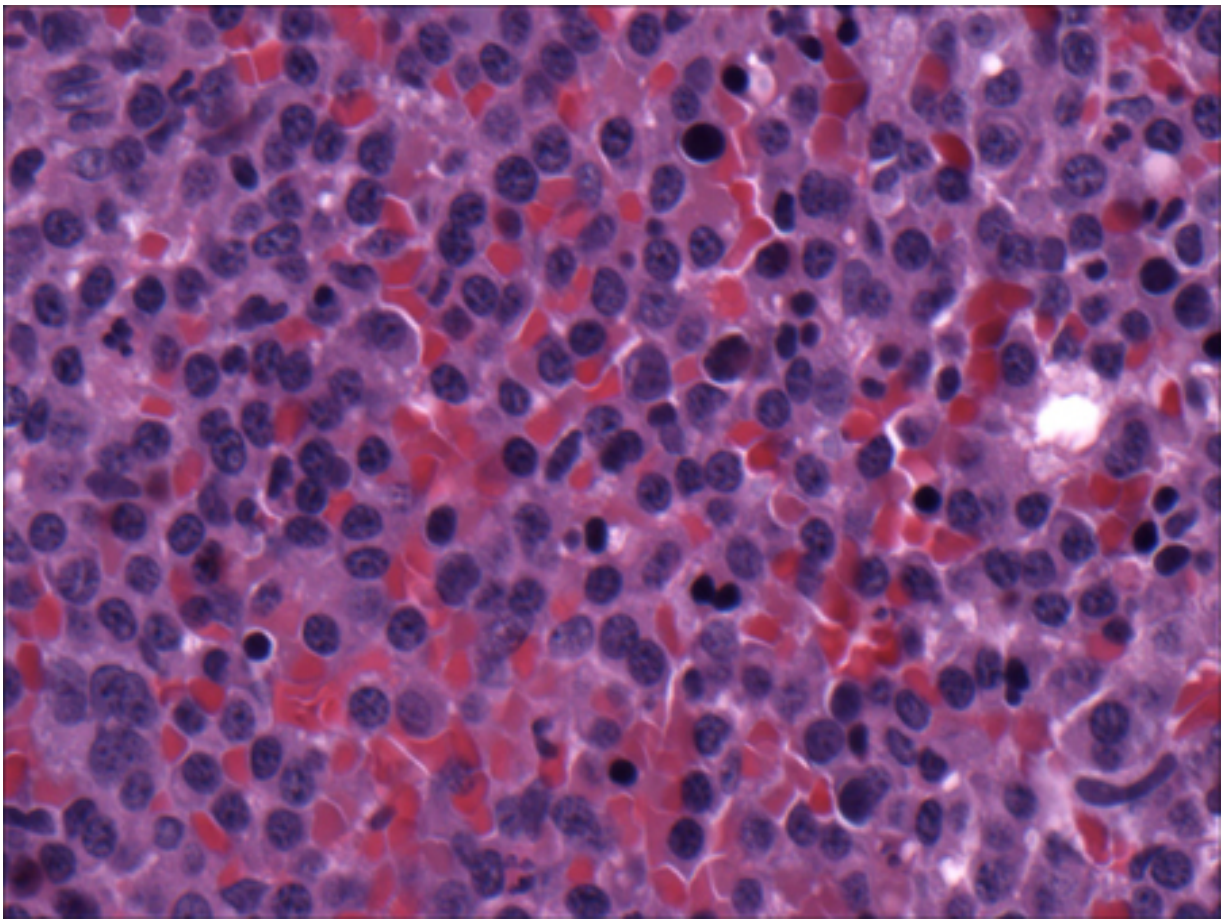


*Figure 4: Multiple myeloma: bone marrow biopsy*

*Courtesy of Dr Robert Hasserjian, Hematopathology, MGH*

IMAGES

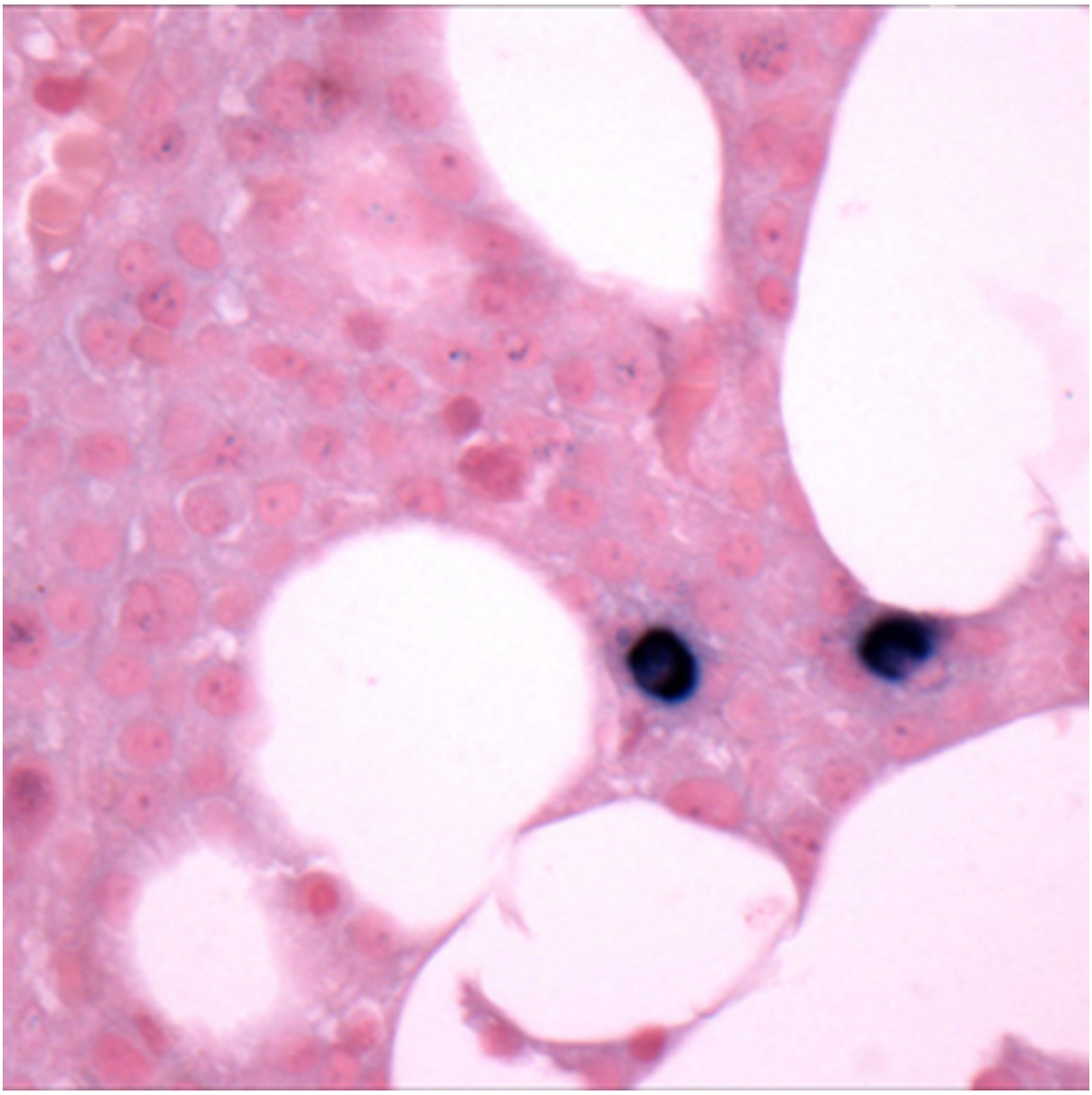


*Figure 5: Multiple myeloma: bone marrow biopsy after histochemical analysis for lambda light chain*

*Courtesy of Dr Robert Hasserjian, Hematopathology, MGH*

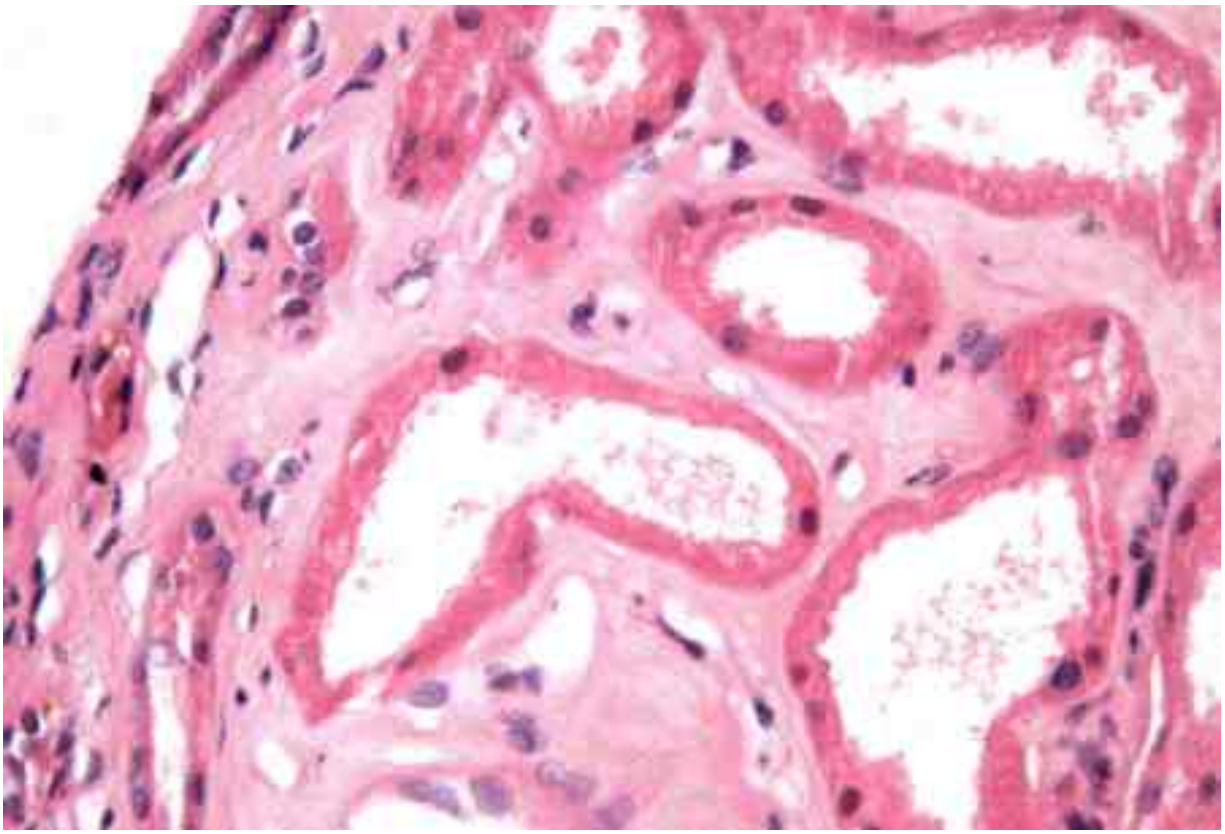


*Figure 6: Acute tubular necrosis: biopsy showing focal areas of proximal tubule vacuolisation and flattening; tubular dilation; brush border debris present in some tubular lumen*

*Courtesy of Puigvert Foundation, Barcelona, Spain*

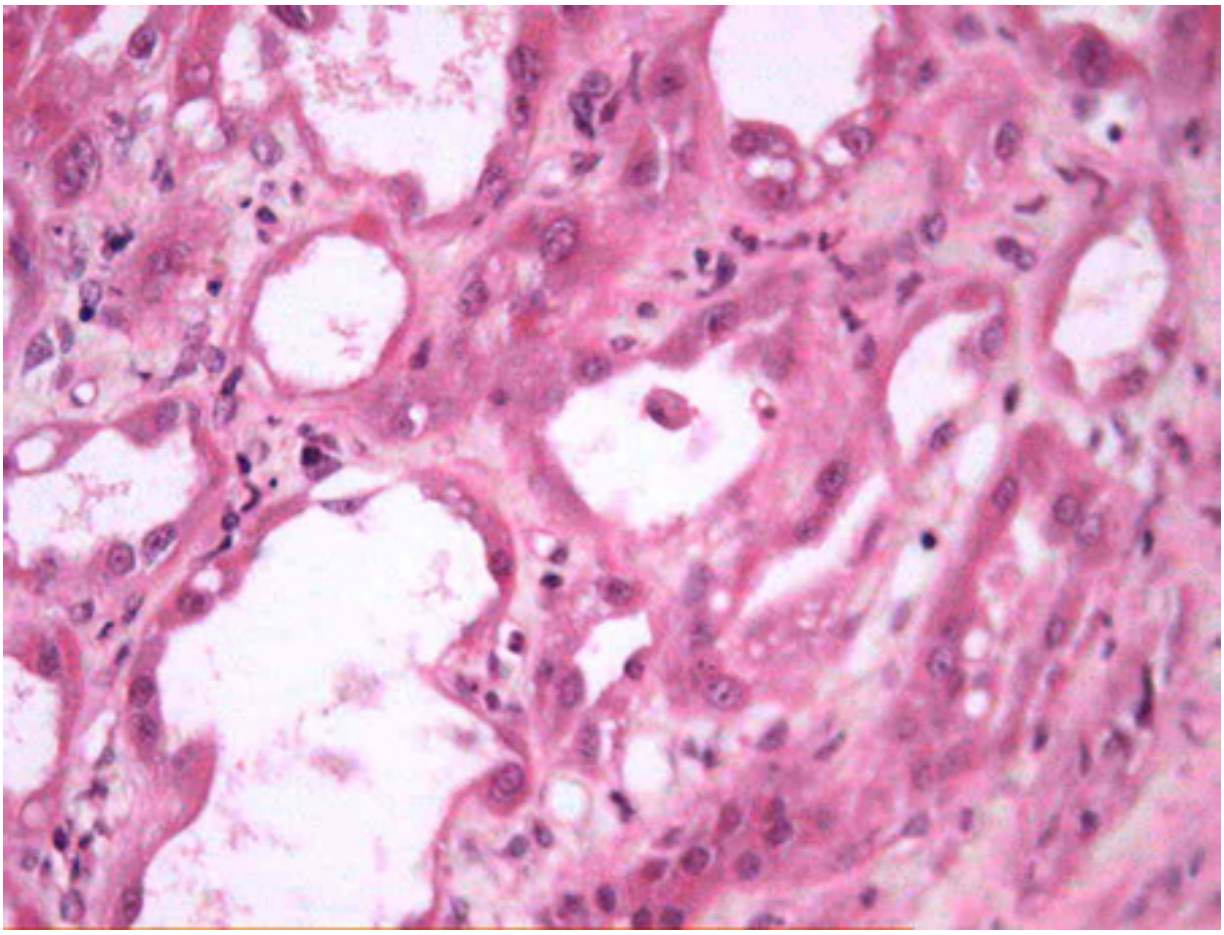


*Figure 7: Acute tubular necrosis: biopsy showing denuded basement membranes and presence of cells in the tubule lumen*

*Courtesy of Puigvert Foundation, Barcelona, Spain*

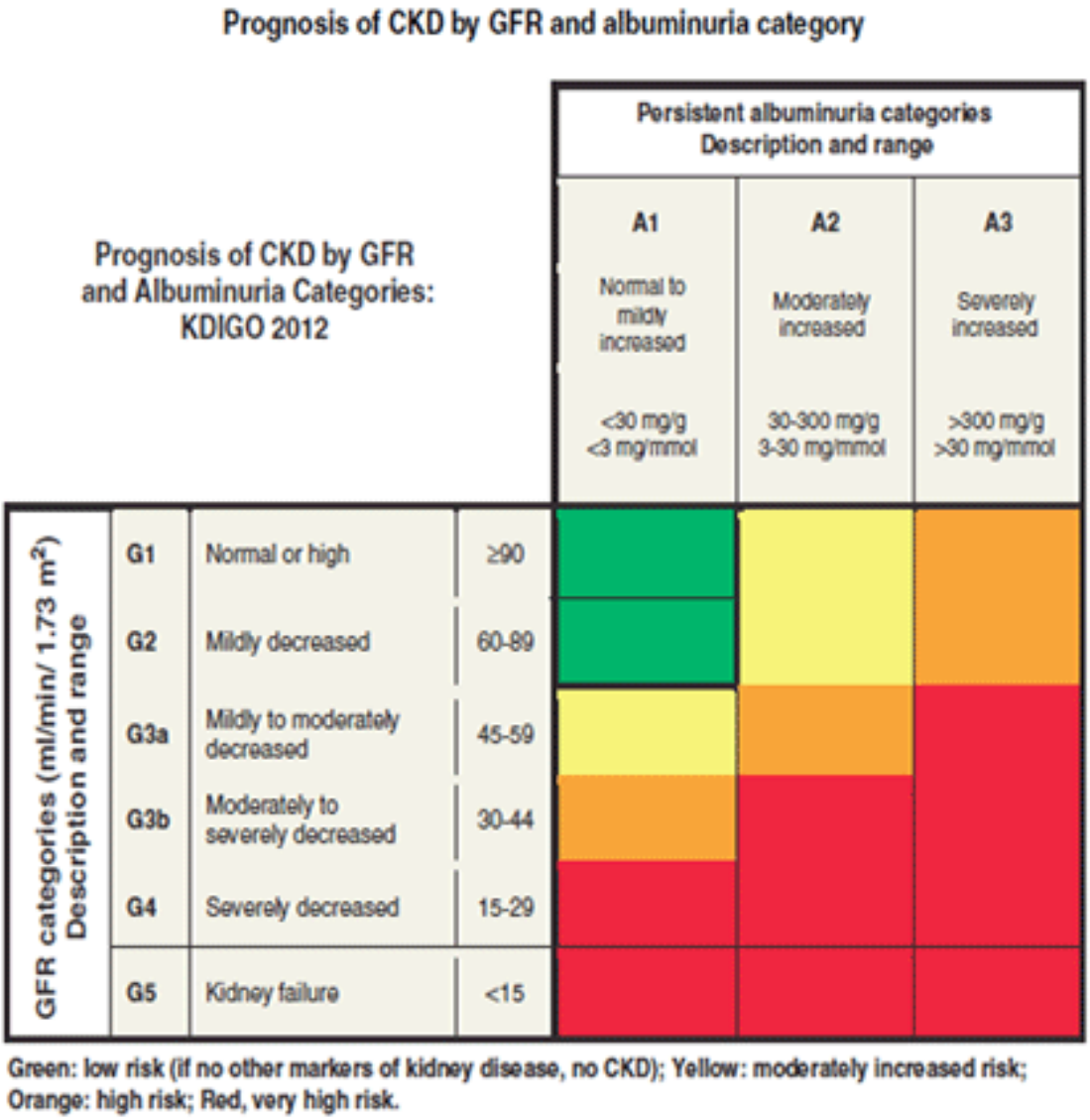



*Figure 8: Prognosis of CKD by GFR and albuminuria category: CKD, chronic kidney disease; GFR, glomerular filtration rate; KDIGO, Kidney Disease Improving Global Outcomes*

# Disclaimer

This content is meant for medical professionals situated outside of the United States and Canada. The BMJ Publishing Group Ltd ("BMJ Group") tries to ensure that the information provided is accurate and up-to-date, but we do not warrant that it is nor do our licensors who supply certain content linked to or otherwise accessible from our content. The BMJ Group does not advocate or endorse the use of any drug or therapy contained within nor does it diagnose patients. Medical professionals should use their own professional judgement in using this information and caring for their patients and the information herein should not be considered a substitute for that.

This information is not intended to cover all possible diagnosis methods, treatments, follow up, drugs and any contraindications or side effects. In addition such standards and practices in medicine change as new data become available, and you should consult a variety of sources. We strongly recommend that users independently verify specified diagnosis, treatments and follow up and ensure it is appropriate for your patient within your region. In addition, with respect to prescription medication, you are advised to check the product information sheet accompanying each drug to verify conditions of use and identify any changes in dosage schedule or contraindications, particularly if the agent to be administered is new, infrequently used, or has a narrow therapeutic range. You must always check that drugs referenced are licensed for the specified use and at the specified doses in your region. This information is provided on an "as is" basis and to the fullest extent permitted by law the BMJ Group and its licensors assume no responsibility for any aspect of healthcare administered with the aid of this information or any other use of this information.

View our full Website Terms and Conditions.

# Contributors:

## // Authors:


**Sana Waheed, MD**

Assistant Professor of Medicine
Medicine/Nephrology, University of Wisconsin School of Medicine and Public Health, Madison, WI
DISCLOSURES: SW declares that she has no competing interests.


## // Acknowledgements:


Dr Sana Waheed would like to gratefully acknowledge Dr Derek M. Fine and Dr C. John Sperati, previous contributors to this monograph.
DISCLOSURES: DMF is an author of a reference cited in this monograph. CJS declares that he has no competing interests.


## // Peer Reviewers:


**Mark Perazella, MD**

Associate Professor
Yale University School of Medicine, New Haven, CT
DISCLOSURES: MP declares that he has no competing interests.

**Arif Showkat, MD, FASN**

Assistant Professor
Division of Nephrology, University of Tennessee, Memphis, TN
DISCLOSURES: AS declares that he has no competing interests.

**Guy Neild, MD, FRCP, FRCPath**

Professor of Nephrology
Institute of Urology and Nephrology, University College London, London, UK
DISCLOSURES: GN declares that he has no competing interests.

**Frederick Tam, MBBS**

Senior Lecturer in Renal Medicine
Division of Medicine, Imperial College London, UK
DISCLOSURES: FT has received travelling grants from Amgen, MSD, Novartis, and Roche to attend International Nephrology conferences. He has also received research grants from Wellcome Trust, Medical Research Council UK, Baxter Biosciences, and Roche Palo Alto. He has also provided consultancy to research work with GE Heathcare and Baxter Biosciences.