

Nephrology in a nutshell

Ulf Schönermarck, Michael Fischereider and
Walter Samtleben

Cardinal symptoms of kidney diseases

Hematuria

Microhematuria

- Only microscopically detectable erythrocytes in the urine,
- $> 2 - 3$ erythrocytes per high-power field (magnification, $400\times$) in the urinary sediment.

Macrohematuria (gross hematuria)

- Visible red or brown (“Coke-like”) discoloration of the urine in case of hematuria, e.g.: IgA nephropathy, nephrolithiasis, renal carcinoma
- DD pigmenturia (hemoglobinuria, myoglobinuria, after consumption of beets).

Dysmorphic erythrocytes

- In cases of renal erythrocyturia deformed erythrocytes ($> 75\%$) may be detected on phase contrast microscopic investigation in the sediment,
- more than 5% acanthocytes (i.e. erythrocytes with vesicle-shaped or bubble-like protrusions) specifically suggest glomerular erythrocyturia,
- in contrast, normal morphology of erythrocytes in non-glomerular or extra-renal erythrocyturia (e.g. in urinary tract infection).

Red blood cell casts

- Erythrocytes included in precipitated Tamm-Horsfall glycoprotein matrix as an indicator of glomerular lesion, virtually diagnostic of GN.

Proteinuria

- Dipstick (caution: primarily detection of albumin, no detection of paraproteins), precipitation by sulfosalicylic acid, urine electrophoresis, nephelometry, immunoelectrophoresis.
- Quantification in a 24-hour urine sample (sample period: Day 1 start after morning urine, Day 2 end after morning urine) or use protein-to-creatinine ratio in a spot urine sample.
- Normal < 100 – 150 mg proteinuria/day; < 3 g/day in a variety of renal diseases including glomerulonephritis, pyelonephritis, interstitial nephritis, nephrosclerosis. > 3.5 g/day (“nephrotic range proteinuria”), e.g. in several types of GN, paraproteinuria, diabetic nephropathy, renal amyloidosis etc.

Pre-renal proteinuria (overflow proteinuria)

- Bence-Jones proteinuria (light-chain proteinuria),
- hemoglobinuria,
- myoglobinuria.

Renal proteinuria

- **selective glomerular:**
mainly albumin; if albuminuria 30 – 300 mg/day = microalbuminuria, e.g. in diabetic nephropathy Stage III, minimal-change GN,
- **non-selective glomerular:**
almost all serum proteins present in urine; in almost all cases of GN
- **tubular:**
usually less than 1 – 1.5 g/day, small proteins < 60 kD, which are physiologically filtered and subsequently reabsorbed by the

tubulus cells.

Isolated appearance in the rare case of a pure tubular damage.
Micromolecules: β_2 - and α_1 -microglobulin, e.g. in aminoglycoside toxicity.

Post-renal proteinuria

- Distributed like serum proteins, e.g. in post-renal hemorrhage, urinary tract infection.
- **Method of detection:**
urinary electrophoresis (SDS-PAGE) and/or nephelometric determination of proteins in the large (IgG), medium (albumin) and small molecular weight range (β_2 - or α_1 -microglobulin).

Edema

- Lid edema in the morning,
- lower leg/ankle edema,
- perhaps pulmonary edema,
- ascites,
- sometimes anasarca.

Pathogenesis

- Sodium and water retention,
- protein deficiency in nephrotic range proteinuria.

Arterial hypertension in kidney disease

- Often rise of systolic and diastolic blood pressure, frequently loss of normal nocturnal decline in blood pressure (“non-dippers”)
- Risk factor for progression of renal insufficiency
- Primary renal disease: acute or chronic renoparenchymatous damage leading to salt and water retention, hyperreninism,

– **Renovascular disease:**

atherosclerotic or fibromuscular renal artery stenosis with activation of the renin-angiotensin-aldosterone system.

Dysuria, leukocyturia, bacteriuria

- Prominent features of upper or lower urinary tract infections (cystitis, PN),
- micturition accompanied by burning pain, costovertebral angle pain and tenderness, fever in cases of PN,
- in cases of germ detection and without symptoms, antibiotic treatment only in cases with co-existing leukocyturia,
- in “sterile leukocyturia” (missing germ detection in gram preparation or on conventional urine culture media): interstitial nephritis (sometimes with eosinophiluria), otherwise search for acid-resistant rods in the morning urine, urethral smear for chlamydia, ureaplasma urealyticum, mycoplasma.

Renal insufficiency

- Decrease in GFR and subsequent increase of serum creatinine. Renal insufficiency may be acute (probably reversible) or chronic,
- Stages of chronic kidney disease as defined by the National Kidney Foundation (NKF-K/DOQI) see Table 1.
- Estimation of glomerular filtration rate (GFR) is based upon the following equations:

MDRD equation

Estimated GFR (ml/min per 1.73m²) =
 $1.86 \times \text{plasma creatinine [mg/dl]}^{-1.154} \times (\text{age [years]})^{-0.203}$

multiply by 0.742 for women

multiply by 1.21 for African Americans

Table 1. Stages of chronic renal disease as defined by the National Kidney Foundation (NKF-K/DOQI).

Stage	GFR (ml/min/1.73 m ²)	Description
1	> 90	kidney damage with normal GFR
2	60 – 89	kidney damage with mild decreased GFR
3	30 – 59	moderate reduced GFR
4	15 – 29	severe decreased GFR
5	< 15 (or dialysis)	kidney failure

The new proposed KDIGO guidelines will include different degrees of proteinuria as well as splitting of Stage 3 into A and B

CKD-EPI equation

Estimated GFR (ml/min per 1.73 m²) =
 $141 \times \min(\text{Scr}/k, 1)^a \times \max(\text{Scr}/k, 1)^{-1.209} \times 0.993^{\text{Age}} \times$
 $1.018 [\text{if female}] \times 1.159 [\text{if black}]$

Scr is serum creatinine, k is 0.7 for females and 0.9 for males, a is –0.329 for females and –0.411 for males, min indicates the minimum of Scr/k or 1, and max indicates the maximum of Scr/k or 1.

Cockcroft-Gault equation

Estimated GFR (ml/min) = $\frac{(140 - \text{age}) \times \text{body weight (kg)}}{72 \times (\text{plasma creatinine [mg/dl]})}$

multiply by 0.85 for women.

Several equations using cystatin C have been developed, e.g.

CKD-EPI cystatin equation adjusted for age, sex, and race:

Estimated GFR (ml/min per 1.73 m²) = $127.7 \times \text{CysC}^{-1.17}$
 $\times \text{age}^{-0.13} \times 0.91 (\text{if female}); \times 1.06 (\text{if African American}).$