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4.1 Definition

Proteinuria is defined as the temporary or continuous detection of proteins in the urine, which exceeds an amount of 150–200 mg per 24 h, using a base of urine production of 1,500 ml a day. Regular protein excretion consists of approximately 30 % globulins, 30 % albumin, and 40 % of other proteins, especially Tamm-Horsfall glycoprotein (uromodulin, excreted primarily by the kidney).

In a healthy kidney, limitation of protein loss is regulated by the glomerular filter, with a filtration barrier for proteins larger than 50 kDa and especially negative electrically charged molecules, and the tubular reabsorption of smaller proteins and amino acids which passed the glomerular membrane. Therefore, proteinuria is subdivided into different categories: glomerular (prevalent heavy molecular weight), tubular (prevalent small molecular weight), overflow (increased serum protein concentrations), and also postrenal proteinuria (increased renal excretion or associated infection). Table 4.1 summarizes typical marker proteins.

Microalbuminuria, characterized as a 30–300 mg loss in 24 h or a urine concentration of 20–200 mg albumin per liter, should be considered in patients with diabetes mellitus and/or hypertension as an early marker for nephropathy.

4.2 Medical History

In most cases proteinuria is not a symptom reported by the patient himself/herself. Generally proteinuria is either found during a preventive medical checkup or identified within specific laboratory urine analysis in case of a suspected diagnosis or

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Table 4.1 Marker proteins to categorize the form of proteinuria

<i>Glomerular proteinuria</i>
Selective glomerular proteinuria
Albumin
Transferrin
Unselective glomerular proteinuria
Albumin
Transferrin
Immunoglobulin G
α -2-macroglobulin
Tubular proteinuria
β -2-microglobulin
Alpha-1-acid glycoprotein
Prerenal proteinuria (“overflow”)
Myoglobin (muscle trauma)
Hemoglobin (hemolysis, also red urine)
Bence Jones protein (paraneoplastic)
Postrenal
Tubular secret proteins, e.g., Tamm-Horsfall

proved disease. Only in rare cases the patient presents with the specific symptom of foaming urine during micturition.

The initial medical history should focus on the timing of proteinuria. In case of short-term proteinuria, typical signs of infection (fever, exudation, dysuria, malaise) and emotional and physical stress should be explored. Especially in young men, intermittent and light proteinuria is often seen as a so-called orthostatic proteinuria, which can be excluded by repeated morning urine sample analysis. In case of persistent proteinuria, a wide range of diseases with nephrotoxic potential are known. Therefore, a comprehensive anamnesis including acute and chronic diseases, as well as cancer with potential paraneoplastic protein production, should be investigated. Advanced proteinuria can lead to hypoproteinemia with a decreased oncotic pressure resulting in edemas and ascites.

4.3 Diagnostics

Dipstick analysis is the first step to detect proteinuria. The dye for protein analysis changes due to a pH shift. Dipstick tests are most sensitive to albumin; therefore, false-negative results could be obtained, if albumin excretion is not increased (e.g., in case of a Bence Jones proteinuria) or if the urine sample is highly diluted or alkaline. Standard dipstick tests will also not detect microalbuminuria.

If proteinuria is present and reasons for short-term proteinuria (especially urinary tract infection) are excluded, a quantification of the amount of protein loss should be performed over a 24-hour period. Protein electrophoresis of the urine unveils the different molecules of proteinuria based on their molecular weight,

which enables the categorization in Table 4.1. If a paraneoplastic “overflow” proteinuria is suspected, immunoelectrophoresis and immunofixation are the methods of choice. Quantification of specific proteins could be achieved either by urine (immuno-) nephelometry or turbidimetry.

In case of continuous proteinuria, urine analysis should be accompanied by the examination of the urine sediment (focus on dysmorphic erythrocytes and urinary casts in case of glomerulonephritis) as well as serum protein analysis.

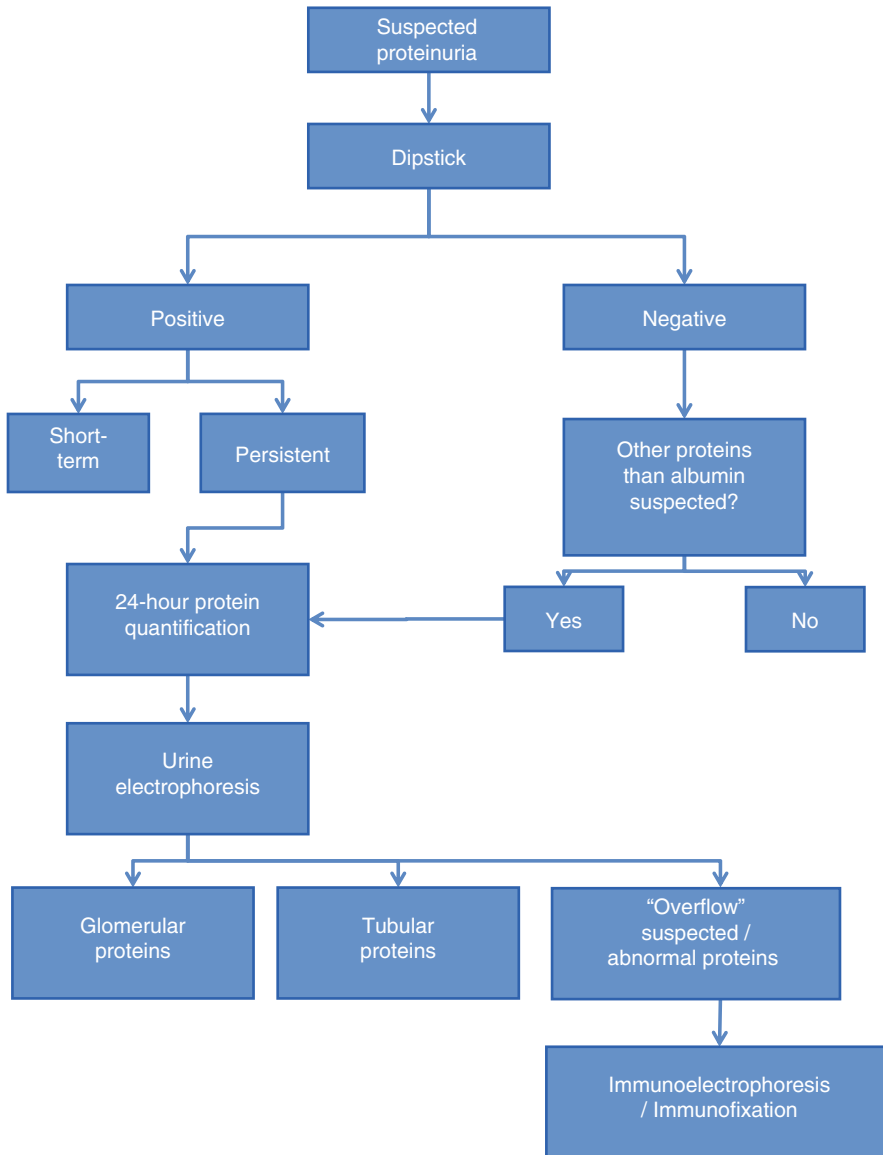


Table 4.2 Examples of different proteinuria-associated diseases

<i>Short-term or intermittent proteinuria</i>	
Prerenal (“overflow”)	
	Orthostatic proteinuria
	Muscle trauma
	Hemolysis
Pre- and/or postrenal	
	Urinary tract infection
	Systemic infections
	Physical/emotional stress
<i>Persistent proteinuria</i>	
Prerenal (“overflow”)	
	Paraneoplastic proteins: multiple myeloma, Waldenström’s macroglobulinemia
	Hemolysis
Glomerular	
	Glomerulonephritis (partially with tubular proteinuria)
	Hypertensive nephropathy
	Diabetic nephropathy (early stage, late stage: plus tubular proteinuria)
	Benign nephrosclerosis
	Nephropathy associated with different forms of systemic vasculitis (plus tubular proteinuria)
	Renal transplant rejection (plus tubular proteinuria)
Tubular	
	Interstitial nephritis
	Analgesic nephropathy
	Fanconi’s syndrome
	Balkan nephropathy
	Tubulotoxic drugs (e.g., aminoglycosides)
	HIV nephropathy

4.4 Differential Diagnosis

Differential diagnoses of proteinuria underlying diseases are summarized in Table 4.2 [1–3].

References

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