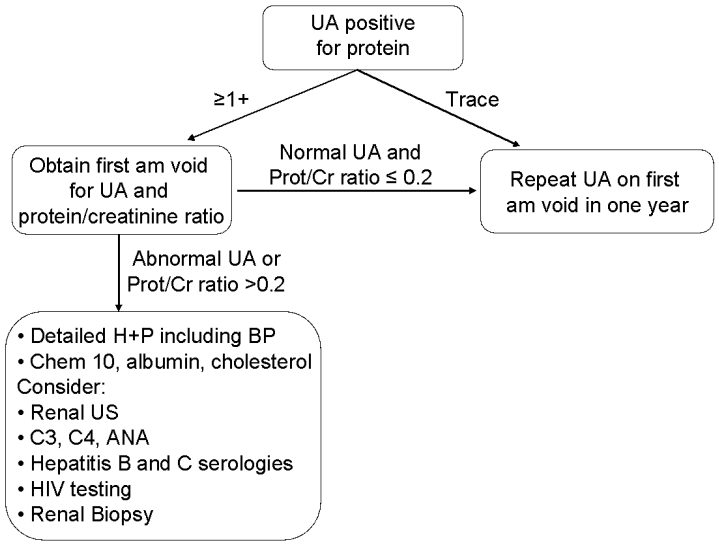
Proteinuria

Definition



Etiology

- **Glomerular** (inc filtration of macromolecules, esp albumin -- may be **transient** [fever, exercise, stress, seizures, resolves on rpt testing after stressor gone] vs **orthostatic** [present when standing and not when supine - first morning void] vs **persistent** [elevated on both supine/upright voids])
- **Tubular** (inc excretion of **low molecular weight proteins**, esp beta-2-microglobulin, that are normally filtered in the glomerulus and reabsorbed in the proximal tubule -- may be d/t congenital disorders of proximal tubule [Fanconi syndrome, cystinosis, galactosemia, Lowe syndrome] or with acute tubular injury [ATN, AIN, pyelo])
- **Overflow** (inc excretion of low molecular weight proteins d/t protein overproduction [multiple myeloma, myoglobin in rhabdomyolysis] .

Presentation

- If significant quantity, protein will be frothy; otherwise varies with cause
- If nephrotic, may have edema/HTN, may have stigmata of primary dx (oral ulcers, rash, and joint swelling in SLE; abdominal pain and palpable purpura in HSP; h/o recurrent UTIs with VUR, hepatitis and movement d/o in Wilson dz)

Nephritic Syndrome

Definition

Any of several conditions leading to glomerular hematuria, proteinuria, and potential AKI with azotemia/oliguria, edema, and hypertension.

Etiology

- Post infectious:
  - **Group A beta hemolytic strep**, either after pharyngitis or impetigo
  - Other infections: staph aureus/epi, pneumococcus, mycoplasma, viral
- IgA Nephropathy (most common glomerulopathy worldwide)
- SLE Nephritis
- **Membranoproliferative GN**: can be idiopathic or secondary to HBV/HCV or rheumatologic disease
- **Alport Syndrome**: XLR collagen IV mutations, a/w hearing loss, vision changes
- **Goodpasture Syndrome**: autoAb to Type IV collagen in glomerular and alveolar basement membranes → hemoptysis,
- **Vasculitis**: HSP, granulomatosis with polyangiitis (lung/sinus/kidney), eosinophilic granulomatosis with polyangiitis (asthma/neuropathy/lung/kidney/skin), microscopic polyangiitis (lung/kidney)

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Nephritic Syndrome	

Clinical Manifestations	• Hypertension
	• Hematuria
	• Fluid retention/edema
	• Sequelae of underlying disease
	  ▪ **SLE**: rash, arthritis, oral ulcers
	  ▪ **Vasculitides**: hemoptysis, skin ulcers
	  ▪ **Alport**: sensorineural hearing loss, vision changes
	• Ask about preceding sore throat (usually 2-3 weeks before onset of post strep GN) or current URI symptoms (which can be seen with IgAN)
	• Some patients may have rapid progression with development of acute renal failure over course of several days. Any of above etiologies can have a rapidly progressive course.

Exam	• Monitor BP • Assess volume status • Look for signs of lupus or other vasculitides such as rash, abdominal tenderness (HSP), joint swelling/tenderness
Diagnostic Studies	• **UA**: RBCs + proteinuria. Glomerular bleeding → dysmorphic RBCs and red cell casts • Chem 10 / CBC/diff/retic / serum albumin / ASLO + anti-DNase B / ANA + anti-dsDNA • **C3, C4**: low C3 seen with post-infectious GN and C3 glomerulopathy low C3/C4 in SLE; normal C3/C4 in IgAN, pauci-immune GNs (ANCA-associated vasculitis) and anti-GBM disease • **Urine protein to creatinine ratio**: typically will see proteinuria, sometimes in nephrotic range (nephrotic range protein is urine protein/Cr ratio >2) • If rapidly progressive course or significant renal insufficiency on admission, send anti-GBM Ab and ANCA (for Goodpasture disease and GPA/MPA). Patients with rapidly progressive course should have renal biopsy.

Treatment	• **Reasons for admission**: hypertension, acute renal failure, volume overload, or electrolyte abnormalities
	• Hypertension typically responsive to diuretics
	• Fluid and sodium restriction during acute phase
	• Patients with RPGN may be treated with pulse dose steroids
	  ▪ Patients with RPGN due to Goodpasture disease, SLE, or GPA/MPA may be treated with steroids, cyclophosphamide, and plasmapheresis
	• Post-infectious GN is typically self-resolving
	  ▪ Patients suspected to have post-infectious GN should have repeat complement studies sent in 8-12 weeks, at which time complement should return to normal. If still hypocomplementemic, consider other diagnosis such as C3 glomerulopathy or SLE

Nephrotic Syndrome	
Definition	Syndrome characterized by presence of heavy proteinuria (albuminuria >3 g/24 hours), hypoalbuminemia (<3.0 g/dL), edema, hyperlipidemia, and thrombotic disease
Etiology	• Minimal change disease (most common in children) • Focal segmental glomerulosclerosis • Membranous Nephropathy • Membranoproliferative GN (may be nephrotic + nephritic) • SLE (may be nephrotic + nephritic)
Pathophysiology	• Abnormalities in glomerular podocytes → increased filtration of proteins, esp **albumin**. Others include clotting inhibitors (Protein C, S, anti-thrombin III) → prothombotic state and immunoglobulins → susceptibility to serious infections. • Increased Na retention and hypoalbuminemia → edema • Decreased oncotic pressure → inc hepatic lipoprotein synthesis → hypercholesterolemia
Clinical Manifestations	• Edema, typically first appears in periorbital tissue/scrotum, then in dependent areas • HTN, HLD, increased risk of VTE • Can present with AKI