

# Evaluation of Proteinuria

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# Normal Protein Excretion

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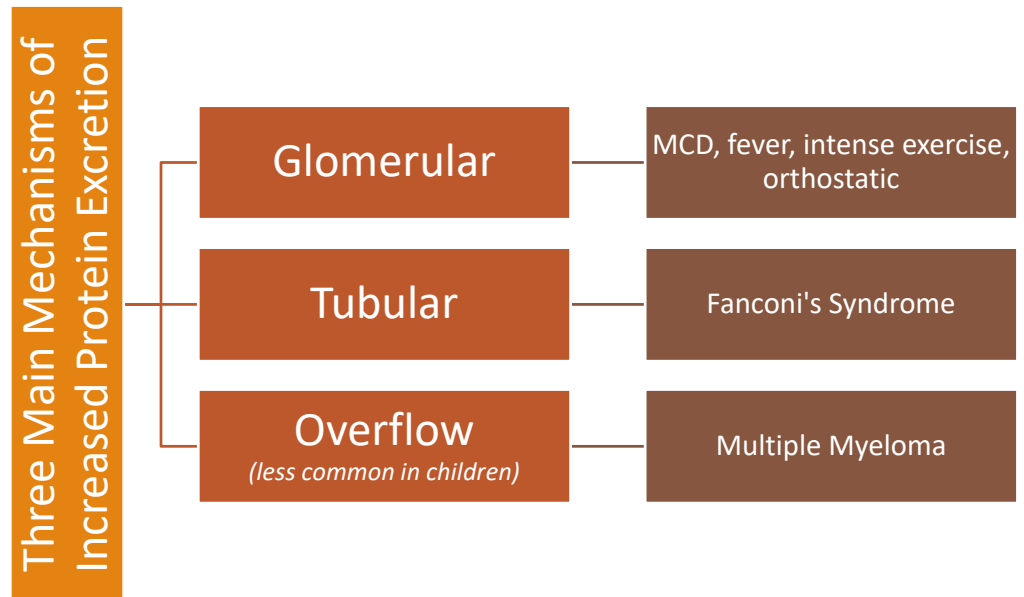
- Urinary protein excretion in the normal child is **less than 100mg/m<sup>2</sup> per day or a total of 150mg per day**
- Urinary protein excretion in neonates is **higher**, up to **300mg/m<sup>2</sup>**, because of reduced reabsorption of filtered proteins
- About half of normal protein excretion are proteins excreted by cells of the **tubular epithelium\***, while the other half consists of **plasma proteins** such as **albumin**, which accounts for 40% of total urinary protein, as well as **LMW proteins** (beta-2-microglobulin, amino acids, etc.)

*\* Only albumin is detected by urine dipstick, while tubular proteinuria is NOT detected*

# Abnormal Protein Excretion

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- Urinary protein excretion in excess of **100mg/m<sup>2</sup> per day** or **4mg/m<sup>2</sup> per hour** is considered abnormal in children
- **Nephrotic range** proteinuria is defined as greater than or equal to **1000mg/m<sup>2</sup> per day** or **40mg/m<sup>2</sup> per hour**



# Measurement of Urinary Protein - Urine Dipstick

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- Most common is the **urine dipstick**, but it only measures the **protein concentration** and cannot be used to quantify protein excretion
  - A dilute urine for example, will underestimate the degree of proteinuria, while a highly concentrated urine may have a protein concentration  $>100\text{mg/dL}$  but not be indicative of increased protein excretion
- Urine dipstick measures the **albumin** concentration
  - Negative
  - Trace – between 15 and 30mg/dL
  - 1+ - between 30 and 100 mg/dL
  - 2+ - between 100 and 300 mg/dL
  - 3+ - between 300 and 1000mg/dL
  - 4+ -  $>1000\text{mg/dL}$
- Urine dipstick with **NOT** measure LMW proteins

# Measurement of Urinary Protein – Quantitative

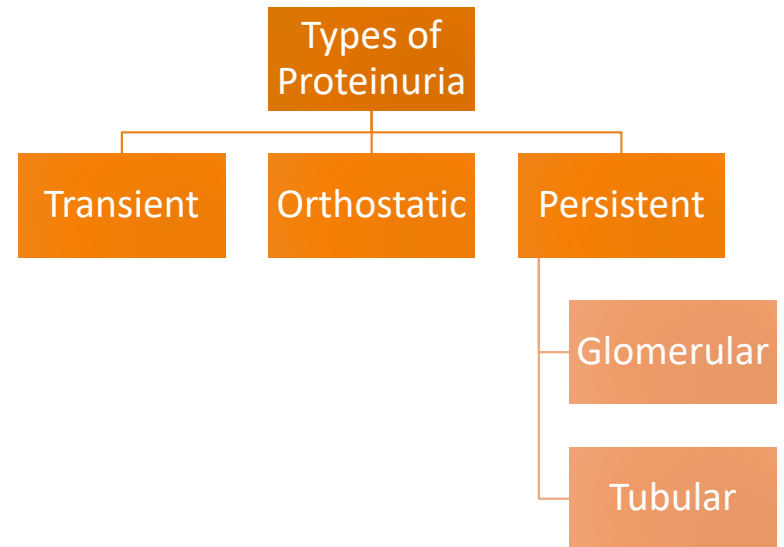
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- If child has **persistent** dipstick-positive proteinuria, they must undergo a quantitative measurement of protein excretion
- It is difficult to obtain an accurate 24-hour collection, so the best alternative is a quantitative **protein/creatinine (Pr/Cr) ratio** on a **spot urine sample**, ideally the first morning specimen
- Normal Ratio: **<0.2mg protein/mg creatinine (<20mg protein/mmol creatinine)** in children greater than 2 years of age

# Approach to the Child with Proteinuria

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- A positive dipstick for protein on a random urinalysis is **common** in children
- General screening of normal school-age children and adolescents with a urine dipstick will be positive (defined as  $\geq 1+$ ) in **5-10%**, however, only **0.1%** of children have persistent proteinuria
- Proteinuria presents in 3 ways – transient, orthostatic and persistent
- Most children will be **asymptomatic**

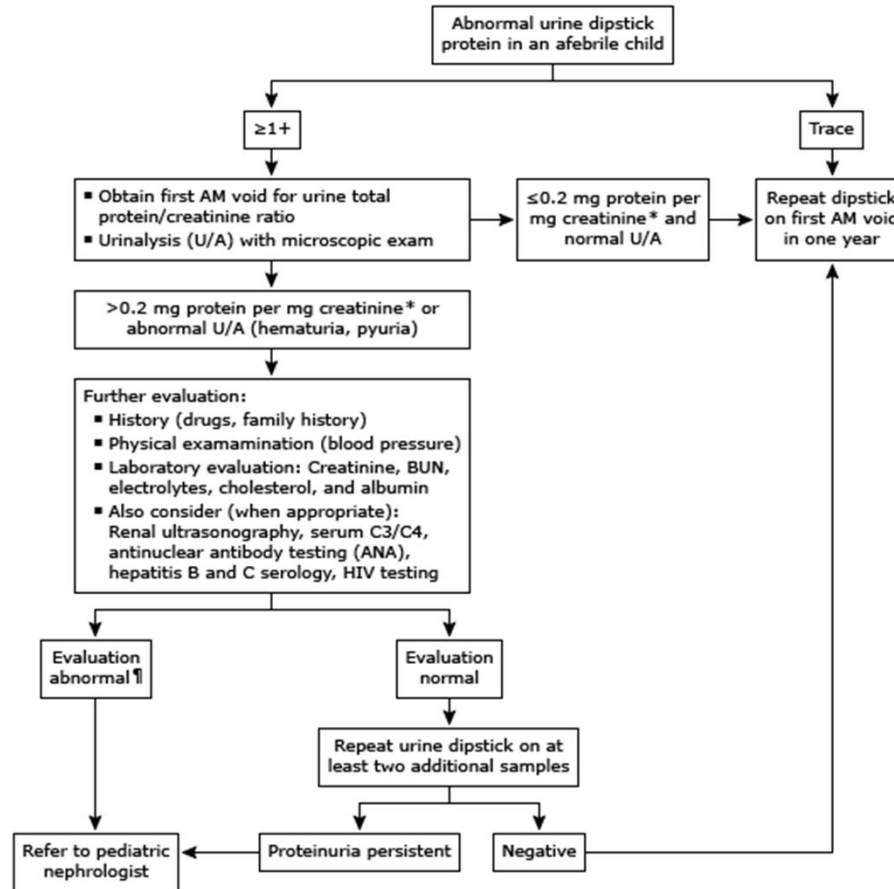


# Approach to the Child with Proteinuria

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- The diagnostic evaluation of the child with dipstick-positive proteinuria depends in part upon the **presence or absence** of symptoms.
- As stated previously, most children are **asymptomatic**
- The following **algorithm** is consistent with the recommendations of the 2000 Pediatric Nephrology panel established at the National Kidney Foundation conference on Proteinuria, Albuminuria, Risk, Assessment, Detection, and Elimination (PARADE)

## Algorithm for evaluation of asymptomatic proteinuria in children





# Types of Proteinuria

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- **Transient Proteinuria** – most common
  - Fever, exercise, stress, seizures, and hypovolemia
- **Orthostatic (or postural) Proteinuria** – defined as increased protein excretion in the upright position which returns to normal when the patient is recumbent.
  - Common cause of proteinuria in adolescent males
- **Persistent Proteinuria** – should be more fully evaluated for underlying renal disease

## Causes of proteinuria in children

<b>Transient proteinuria</b>
Associated with fever, exercise, seizures and/or hypovolemia
<b>Orthostatic proteinuria</b>
<b>Persistent proteinuria</b>
<b>Glomerular proteinuria</b>
Primary
Minimal change disease
Congenital nephrotic syndrome
"Finnish-type"
Mesangial sclerosis
Focal segmental glomerular sclerosis
IgA nephropathy (Berger's disease)
Membranoproliferative glomerulonephritis
Membranous nephropathy
Alport syndrome
Secondary
Acute post-streptococcal glomerulonephritis
Diabetes mellitus
Systemic lupus erythematosus
Henoch-Schönlein purpura
<b>Tubular proteinuria</b>
Primary
Cystinosis
Dent's syndrome
Wilson's disease
Lowe's syndrome
Polycystic kidney disease
Mitochondrial disorders
Secondary
Heavy metal poisoning
Acute tubular necrosis
Tubulointerstitial nephritis
Secondary to obstructive uropathy

# Workup

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- Vital Signs - particularly blood pressure, since hypertension may be indicative of underlying disease
- Repeat urine dipstick and protein/creatinine (Pr/Cr) ratio on first morning spot urine sample
- Urinalysis (UA)
  - UTI rule-out
  - Ketones, glucose
  - Blood
- Renal U/S
- CMP
- C3 and ASO titers, if suspecting post-streptococcal glomerulonephritis (hematuria, HTN, etc.)
- C3, C4 and ANA, if suspecting lupus nephritis (joint pains, rashes, hematologic abnormalities)
- Hepatitis B and C, if concerned for liver disease
- HIV testing

# Sources

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- Gillion Boyer, O., Niaudet, P., Drutz, J., and Kim, M. *Evaluation of proteinuria in children*. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on June 7, 2020).
- Ronald J. Hogg, Ronald J. Portman, Dawn Milliner, Kevin V. Lemley, Allison Eddy, Julie Ingelfinge. *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* Jun 2000, 105 (6) 1242-1249; DOI: 10.1542/peds.105.6.1242
- Bernarda Viteri, Jessica Reid-Adam. Hematuria and Proteinuria in Children. *Pediatrics in Review* Dec 2018, 39 (12) 573-587; DOI: 10.1542/pir.2017-0300