Glomerular Disease

In health, the glomerulus prevents passage of significant amounts of proteins due to small pores and a negative charge. Some small molecular weight proteins that are able to pass through the healthy glomerulus are taken up by renal tubular epithelial cells and undergo lysosomal degradation. Protein uptake is a receptor-mediated process and is saturable.

Proteinuria

- Abnormal amounts of protein in the urine
- May indicate kidney damage if the cause is renal proteinuria

Localizing Proteinuria

- Pre-renal
    - Small molecular weight proteins that fit through a healthy glomerulus
    - Hemoglobin
    - Myoglobin
    - Bence-Jones proteins (humans)
- Renal
    - Functional (transient)
        - Resolves once the underlying condition resolves
        - Fever
        - Seizures
        - Excess cortisol (iatrogenic / Cushing's disease)
        - Hypertension
    - Pathologic
        - Due to lesions within the kidney
        - Glomerular
            - Protein due to damaged glomerulus that allows the abnormal passage of proteins
        - Tubular
            - Proteinuria due to decreased uptake by damaged tubular epithelial cells
    - Post-renal
        - Due to entry of proteins into the urine AFTER it enters the renal pelvis (ureter, bladder, prostate, urethra)
        - Cystitis
            - Bacterial infection
            - Stones
        - Bladder mass / Tumors
        - Prostatic disease

        - Hematuria
            - Resolves if the underlying cause is treated

Importance of Proteinuria

- May indicate an underlying kidney disease (if renal proteinuria)
    - Tubulointerstitial
    - Primary glomerular
    - Both tubulointerstitial and glomerular
- Persistence and degree of renal proteinuria correlate with CKD progression
- Treatment of proteinuria has correlated with a slower progression of CKD

Consequences of Proteinuria

- Development and progression of renal tubular disease and azotemia
    - Nephrotoxic effects of albumin
        - Bound substances, excess albumin uptake
    - Hypertension
- Hypoalbuminemia
    - Edema/Ascites
        - Interstitial fluid overload with hypovolemia
    - Alterations in drug metabolism

Clinical Consequences

- Alteration in coagulation
    - Risk of thromboembolic disease as anti-thrombin is lost
- Development of hyperlipidemia
    - Overproduction by liver
    - Colloidal effects
- Nephrotic Syndrome
    - Indicates a more severe PLN
        - Hypoalbuminemia
        - Proteinuria
        - Hypercholesterolemia
            - Increased production from the liver
        - Edema and/or ascites

Detection of Proteinuria

- Urinalysis and urine dipstick
    - Lower limit of detection 30 mg/dL
    - Microalbuminuria is not detected
- False positives and false negatives may occur so interpret this in light of USG

- Protein negative on urinalysis indicates no need for further testing
- USG
    - "expect" more protein in concentrated urine
    - UPC ratio is NOT affected by urine concentration
- Urine sediment
    - Pyuria, hematuria
    - Urine culture should be run before pursuing a workup for proteinuria
- Urine-Protein-Creatinine-Ratio
    - More accurate than a dipstick
    - Not impacted by USG
    - Variation in patient's daily UPC
    - > 2 UPC measurements should be made to determine if proteinuria is transient or persistent (recheck in 2-4 weeks)

Renal Proteinuria

- Once pre- and post-renal proteinuria have been ruled out and there is still proteinuria, it is likely renal proteinuria
- Significant glomerular proteinuria can be present without azotemia!

Tubular vs Glomerular Renal Proteinuria

- If you suspect a primary glomerular problem, consider if there is an immune component
- Treatment for immune-mediated and non-immune mediated PLN will be the same EXCEPT for the use of immunosuppressive drugs
- Rule out IMHA, TIP, IMPA

Note: In patients with severe hypoalbuminemia, they can develop interstitial edema (interstitial overhydration) but have decreased vascular volume

Breed predispositions

Lyme Nephritis: Labs, Goldens, Shetland Sheepdogs

Familial PLN: Soft Coated Wheaten Terriers

Renal Amyloidosis: Shar-Pei

Treatment of Proteinuria

- Treat hypertension
    - Amlodipine
    - ACE*i* *Initial treatment*
        - Prevents constriction of efferent arteriole

        - Decreases pressure across glomerulus and decreases protein loss in the tubule
        - May lead to progressive azotemia and hyperkalemia
    - Angiotensin II receptor blocker (Telmisartan)
        - Synergistic with ACE*i*
        - Alternate effect on RAAS
    - Omega-3 Fatty Acids
    - Anti-platelet drug (AFTER biopsy)
        - Clopidogrel
    - Treat and recheck until goal BP is obtained

Renal Biopsy

- Primary goal is to evaluate for underlying immune-mediated disease

Obtaining a renal biopsy

    - Ultrasound-guided
        - Tru-cut
    - Laparoscopic
    - Laparotomy
- Risks
    - Hemorrhage
        - Increased risk with hypertension
        - More severe azotemia
        - When biopsy extends past the medulla
        - Recent anti-platelet drug administration
        - *NO ACE*i* the night before!
- Evaluating results
    - Ideal to send to a nephropathologist
    - Various stains and interpretation needed

Treatment for Immune-Complex Glomerulonephritis

- Various immune-mediated protocols have been implemented but mycophenolate is most common. Corticosteroids are not typically used due to their increased risk for hypertension and thromboembolic disease

Overview

Evaluate proteinuria with urinalysis to localize and rule out obvious post- and pre-renal causes

Once renal proteinuria is suspected, perform a UPC

Evaluate the degree of proteinuria