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Clinical Approach to Proteinuria

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Definition and Importance

- Albumin, globulins, Bence Jones, etc
- Clue to another underlying disease
- Progression of chronic kidney disease (CKD)
- Increased morbidity and mortality

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Testing

- Urinalysis (dipstick; colorimetric reagent strip)
- Sulfosalicylic acid (SSA)
- Microalbuminuria
- Urine Protein to Creatinine Ratio (UPCR)



Types of Proteinuria

- **Pre-renal**
 - Hemoglobinuria
 - Myoglobinuria
 - Immunoglobulinuria (neoplasia)
- **Post-renal**
 - UTI
 - Urinary tract neoplasia
 - Urolithiasis
 - Cystitis
- **Renal**
 - Functional (transient) vs Pathological (renal lesions)



Investigation of Proteinuria

- **Verification**
 - USG >1.030 or pH >7.5 (<1+)
 - Repeat UA
- **Localization**
- **Persistence**
- **Magnitude**



Localization — Rule Down Pre-renal

- **CBC**
 - Anemia
 - Spherocytosis
- **Chemistry**
 - Hyperglobulinemia
 - Creatinine Kinase (CK)
 - Total Bilirubin
- **+/- Thoracic/Abdominal Radiographs**



Localization — Rule Down Post-Renal

- **History and physical exam**
 - Rectal
 - Lower urinary tract signs?
- **Urine sediment examination via cystocentesis**
 - Active sediment
- **Urine culture**
- **Abdominal radiographs/ultrasound**



Localization - Renal

- **Blood pressure**
- **UPCR**
- **Vector-borne disease testing**
- **Abdominal ultrasound**
- **Cushing's screening**
- **Dental?**
- **Kidney Biopsy**



Persistence

- **Recheck UPCR**
 - Every 2-3 weeks
 - 3 consecutive readings



Magnitude

- **UPCR not UA/SSA/Microalbuminuria**

- **Transient vs tubular vs renal**
 - >2.0 UPCR?

UP/C value		Substage
Dogs	Cats	
<0.2	<0.2	Non-proteinuric
0.2 to 0.5	0.2 to 0.4	Borderline proteinuric
>0.5	>0.4	Proteinuric

- **Progression of CKD**

- **Monitor vs Investigate vs Intervene**



Iris-kidney.com

Monitor/Investigate/Intervene

- **Monitor**
 - Unexpected finding
 - Mild
 - Easily explained, benign, treatable cause
- **Investigate**
 - Moderate to severe
 - Unexplained disease
- **Intervene**
 - Severe proteinuria
 - Hypoalbuminemia
 - Edema
 - Hypercholesterolemia



Renal Biopsy

- **Open laparotomy**
- **Laparoscopy**
- **Ultrasound-guided**

- **Ohio State University - International Veterinary Renal Pathology Service**
 - Light microscopy
 - Transmission electron microscopy
 - Immunofluorescence



Therapeutic Intervention

- **Treat the underlying disease**
 - Antibiotics
 - Surgery
 - Chemotherapy
 - Dental
 - Trilostane
 - Anti-hypertensives

- **Glomerular disease?**



Glomerular Disease Therapy

- **Diet**
 - Modified protein
 - Polyunsaturated Fatty Acids (PUFA)
- **Medical**
 - ACE inhibitors
 - Enalapril – initial: 0.5 mg/kg q12h; max: 2.0 mg/kg q12h
 - ARB
 - Telmisartan – initial: 1.0 mg/kg q24h; max: 2.0 mg/kg q24h
 - Immunosuppression/modulation (mycophenolate +/- prednisone)
 - Anti-thrombotics (low-dose aspirin or clopidogrel)
 - Diuretics (nephrotic syndrome/edema/effusion)



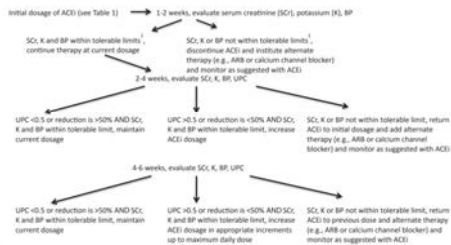
Therapeutic Monitoring

- **Side effects**
 - ACEi and ARB – hypotension, acute kidney injury, hyperkalemia
 - Mycophenolate – vomiting/diarrhea, liver toxicosis, bone marrow
 - Prednisone - pu/pd/pp, worsening proteinuria, hepatomegaly, etc
- **Success**
 - No response
 - Partial Response (<50% reduction)
 - Complete Response (UPCR <0.5)



Therapy Adjustment

Making Adjustments to RAAS Inhibition Therapy in Dogs with Glomerular Disease



Consensus Recommendations for Standard Therapy of Glomerular Disease in Dogs, Brown et al. JVM 2013

Use of Immunosuppressives

- **Biopsy confirms glomerular origin (particularly immune-mediated)**
- **When renal biopsy is not elected and:**
 - Minimal evidence of pre/post/transient renal
 - Immunosuppression is not contraindicated
 - Familial nephropathy is not expected
 - Low suspicion of amyloidosis
 - Breed, family, deposition in other organs
- **Non-responsive to diet/RAAS inhibition with moderate/severe azotemia or severe hypoalbuminemia**



Risks of Immunosuppressives

- Infection
- Worsening of proteinuria (prednisone)
- Individual drug side effects
 - Mycophenolate – diarrhea, vomiting, anorexia, liver toxicity
 - Cyclophosphamide – bone marrow suppression, GI, sterile hemorrhagic cystitis
 - Prednisone – pu/pd/pp, muscle loss, weakness, hepatomegaly
 - Azathioprine – bone marrow suppression, liver toxicity, pancreatitis
 - Cyclosporine – GI, anorexia, bone marrow suppression, liver toxicity



Summary

- Verify presence
- Localize: Pre/Post/Transient/Renal
- Verify persistence
- Determine magnitude

- Monitor vs Investigate vs Intervene

- Therapeutic monitoring is extremely important!



Suggested Reading

Assessment and Management of Proteinuria in Dogs and Cats: 2004 ACVIM Forum Consensus Statement (Small Animal)

George E. Lees, Scott A. Brown, Jonathan Elliott, Gregory F. Grauer, and Shelly L. Vaden

Consensus Guidelines for Immunosuppressive Treatment of Dogs with Glomerular Disease Absent a Pathologic Diagnosis

IRIS Canine GN Study Subgroup on Immunosuppressive Therapy Absent a Pathologic Diagnosis,
B. Pressler, co-chair, S. Vaden, co-chair, B. Gerber, C. Langston, and D. Polzin

Consensus Recommendations for Standard Therapy of Glomerular Disease in Dogs

IRIS Canine GN Study Group Standard Therapy Subgroup, S. Brown, chair, J. Elliott, T. Francey,
D. Polzin, and S. Vaden



Questions?

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