Consensus Statement
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Consensus Recommendations for the Diagnostic Investigation of Dogs with Suspected Glomerular Disease

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Background: The International Renal Interest Society (IRIS) offers guidelines for chronic kidney disease and acute kidney injury. As dogs with glomerular disease may present differently and require different treatment than those with whole nephron or tubular disease, the IRIS Canine Glomerulonephritis (GN) Study Group was convened to formulate guidelines for these cases. The Diagnosis Subgroup was asked to make recommendations for diagnostic evaluation of such cases.

Objective: To seek consensus among renal specialists for the evaluation of dogs with proteinuria because of suspected glomerular disease.

Methods: After reviewing the literature, subgroup members discussed and wrote the draft paper and recommendations, which members of the IRIS Canine GN Study Group voted upon by electronic secret ballot, with comments noted. Consensus was declared if votes showed strong or general agreement from 85% of the respondents.

Results: Diagnostic tests were categorized as essential, recommended, or potentially helpful, with prioritization dependent on case characteristics, eg, for cases with uncomplicated proteinuria versus complicated with hypoalbuminemia, azotemia, or both. Consensus was reached with 86–100% agreement on all questions posed. All cases should have basic examinations including blood pressure measurement, blood, and urine testing, and a search for infectious diseases relevant to their environs. The majority ranked imaging (chest radiographs, abdominal ultrasonogram) and renal biopsy procured and interpreted by experienced personnel as essential evaluations in complicated cases, but a few respondents deemed these to be essential in uncomplicated cases as well.

Conclusions and Clinical Importance: Strong consensus about recommendations for diagnostic evaluation of dogs with suspected glomerular protein loss was attained. These guidelines help clinicians characterize disease processes for more informed therapeutic decision-making.

Key words: Canine; Glomerulonephritis; Glomerulopathy; Protein-losing nephropathy; Proteinuria.

We define primary glomerulopathies as those nephropathies that arise with involvement of glomeruli in the processes that initiate renal injury, regardless of their pathologic mechanism(s), whereas secondary glomerular changes occur after renal tubular or whole nephron damage. In contrast, in human medicine, the term "primary" glomerular disease connotes disease which primarily involves the kidney and "secondary" glomerular disease indicates a disease in which kidney involvement is part of a systemic disorder.[1–3] In any case, diagnostic evaluation of suspected glomerular diseases in dogs is intended to expose the clinical pathological features that will serve as the basis for categorizing dogs with glomerular diseases in ways that will facilitate the formulation of appropriate therapeutic recommendations for these patients.

Proteinuria is an acknowledged hallmark of glomerular lesions in dogs, but proteinuria is not always attributable to renal, much less glomerular, disease. Consequently, when proteinuria is detected, it first must be properly assessed to determine its potential clinical significance. This is a crucial step, the description of which is provided elsewhere and is beyond the scope of this discussion.[4–6] However, proteinuria requires investigation of 3 key elements (localization, persistence, and magnitude), and often it is the

Abbreviations:

ANA	antinuclear antibody
CKD	chronic kidney disease
GN	glomerulonephritis
GWAS	genome-wide association study
Hx	history
IF	immunofluorescence microscopy
IRIS	International Renal Interest Society
LM	light microscopy
PE	physical examination
PLN	protein-losing nephropathy
SDS-PAGE	sodium dodecyl sulfate-agarose gel electrophoresis
TEM	transmission electron microscopy
UPC	urine protein/creatinine ratio
USG	urine specific gravity

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identification of persistent renal proteinuria (see Additional Comments below) by this investigation that causes a suspicion of glomerular disease to arise. Nonetheless, persistent renal proteinuria is not always a marker of glomerular disease. Renal proteinuria, albeit of low magnitude, can be caused by tubular lesions alone, and even when proteinuria is largely of glomerular origin, the glomerular lesions are not necessarily caused by an intrinsic glomerular disease. As repeatedly shown by the results of studies of canine chronic kidney disease (CKD) initiated by partial renal ablation (ie, the remnant kidney model), maladaptive compensatory responses of the surviving nephrons in dogs with CKD typically induce subsequent glomerular changes manifested in part by proteinuria of mild-to-moderate magnitude.[7–9]

In addition, the clinicopathologic manifestations of various glomerular diseases in dogs are diverse and each ranges over a wide spectrum of severity. Consequently, recommendation of a single set of guidelines for diagnostic evaluation of all dogs with suspected glomerular disease, regardless of its evident manifestations, is not appropriate. That is, what is reasonable to recommend for investigation of glomerular disease in an otherwise healthy dog with proteinuria alone differs from what should be done for a dog with proteinuria, azotemia, hypoalbuminemia, hypertension, and edematous extremities (for example).

Table 1. Descriptions of tiers recommended for grouping dogs with glomerular diseases.[a]

Tier I—Persistent renal proteinuria without hypoalbuminemia or azotemia
Tier I-A—Persistent subclinical renal proteinuria that is not accompanied by any discernible renal-related signs or sequellae
Tier I-B—Persistent renal proteinuria with hypertension as the only discernible renal-related sign or sequella, with or without evidence of target organ damage
Tier II—Renal proteinuria associated with hypoalbuminemia, but not azotemia
Tier II-A—Persistent renal proteinuria with hypoalbuminemia, with or without any of its associated complications or sequella (mainly edema and thromboembolic events), but without hypertension or azotemia
Tier II-B—Persistent renal proteinuria with hypoalbuminemia, with or without any of its associated complications/sequella (mainly edema and thromboembolic events), plus hypertension (with or without evidence of target organ damage), but without azotemia
Tier III—Renal proteinuria associated with renal azotemia
Tier III-A—Renal proteinuria with renal azotemia, but not hypertension or hypoalbuminemia
Tier III-B—Renal proteinuria with renal azotemia and hypertension (with or without evidence of target organ damage), but without hypoalbuminemia
Tier III-C—Renal proteinuria with renal azotemia and hypoalbuminemia with or without any of its associated complications/sequella (mainly edema and thromboembolic events), which often (but not always) are accompanied by hypertension (with or without evidence of target organ damage)

[a]Apply tier classification criteria after initial patient stabilization including correction of dehydration, if present.

Recommendation 1:
To facilitate matching diagnostic recommendations to each patient's clinicopathologic circumstances, we recommend separating dogs with glomerular diseases into several different tiers based on the clinical manifestations of their disease when the investigation is conducted.

96% of voting consensus members agreed with Recommendation 1 and 57% of these voters expressed "strong agreement."

Recommendation 2:
Tiers are recommended for grouping dogs with glomerular diseases into categories based on major clinical manifestations of the disease to appropriately match diagnostic recommendations to each dog's clinicopathologic circumstances (Table 1).

86% of voting consensus members agreed with Recommendation 2, and 47% of these voters expressed "strong agreement."

Recognizing that the importance or utility of particular tests or diagnostic procedures is not equal and varies with the contextual circumstances, we here offer prioritized recommendations for the appropriate diagnostic evaluation of suspected glomerular diseases in dogs. In principal, each test or procedure is intended to serve at least one of three broad purposes:

- To identify an underlying disease or condition (eg, infectious, inflammatory, immune-mediated, vascular, neoplastic, endocrine, toxic, or genetic causes) that might be causing the glomerular injury;
- To detect and assess the severity of various glomerular disease sequella (eg, azotemia, hypertension, hypoalbuminemia, hypercoagulopathy, nitrogen and fluid balance) particularly those that might require independent medical management; and
- To characterize the pathologic changes in the kidneys as a means to better inform the attending clinician about the diagnosis, prognosis, and therapeutic options for the glomerulopathy itself.

Recommendation 3:
Particular diagnostic testing or procedures should be assigned a specific hierarchy of importance dependent on the contextual circumstances including clinical severity, resources, expertise, finances, and client willingness (Table 2).

100% of voting consensus members agreed with Recommendation 3, and 59% of these voters expressed "strong agreement."

Table 2. Description of terms used to categorize diagnostic tests and procedures in a hierarchy reflecting their relative importance or utility in the specified situation.

Essential—considered the minimum diagnostic assessment(s) with the highest priority regardless of financial or coexistent clinical circumstances
Recommended—suggested to be what should *always* be done, resources permitting
Potentially helpful—diagnostic assessments that might be performed in specific circumstances to be completely thorough or for investigational or academic analyses

Guidelines for Diagnostic Testing

Recommendations for diagnostic testing are summarized in Boxes 1, 2, and Table 3. Many of the recommendations, particularly those in Box 1, also are components of investigations of proteinuria that are needed to localize its origin and assess its persistence and magnitude, and therefore might already have been performed.

Recommendation 4:
A select group of diagnostics should be recommended in all cases with suspected glomerular disease (Box 1).

95% of voting consensus members agreed with recommendation 4 and 43% of these voters expressed "strong agreement."

Recommendation 5:
Additional diagnostics are recommendations for dogs with suspected glomerular disease associated with high magnitude (UPC $\geq$3.5) or progressive proteinuria, hypertension, hypoalbuminemia, and/or azotemia (Box 2).

95% of voting consensus members agreed with Recommendation 5 and 43% of these voters expressed "strong agreement."

Recommendation 6:
Diagnostic priorities should be based on canine glomerular disease tier (Table 3).

86% of voting consensus members agreed with Recommendation 6 and 42% of these voters expressed "strong agreement."

Additional Comments

Repeating UPC Determinations

Repeated UPC determinations are needed in most situations, regardless of whether the initial observation

Box 1
Consensus Diagnostic Recommendations for All Cases with Suspected Glomerular Disease

Comprehensive history (Hx) including signalment, family, environs, exposures, etc.
- Consider breed predispositions, eg, for glomerular disease, neoplasia, Cushing's disease
- Consider environs or travel-associated infectious diseases that might cause glomerular disease, eg, Lyme disease, heartworm, Ehrlichiosis, Leishmaniasis
- Consider drug or diet exposures that can cause hypertension or glomerular disease, eg, phenylpropanolamine, steroids, raw-food diet, sulfonamides, tyrosine kinase inhibitors

Complete physical examination (PE) including body condition score, retinal and rectal examinations

Blood pressure measurements
- Readings on at least 2 occasions on different days are generally required[10]
- A reliable elevated blood pressure measurement found on a single occasion may be adequate to initiate treatment if found in conjunction with target organ damage consistent with hypertension[10]

Blood and urine testing
- CBC (including platelets)
- Biochemical profile (including BUN, creatinine, phosphorus, calcium, sodium, potassium, albumin, globulin, glucose, alanine transaminase, alkaline phosphatase, bilirubin, cholesterol, and if possible, enzymatic CO_2)
- Urinalysis (including urinary sediment evaluation)
- Urine protein/creatinine ratio (UPC, at least 2 readings, see Repeating UPC Determinations below)
- Urine culture, if warranted, eg., if microscopic pyuria, hematuria, or bacteriuria, USG<1.025, azotemia, or suspected hyperadrenocorticism, diabetes, etc. exists, with possible occult infection

If living in an endemic area or travel history warrants, rule out the common diseases associated with glomerulonephritis characteristic for the area, eg, Lyme disease, heartworm, and Ehrlichiosis in endemic areas in the United States and Ehrlichiosis and Leishmaniasis in southern Europe/Mediterranean regions (see Searching for Infectious Disease below).

Appropriate, problem-specific investigation of any concomitant extrarenal diseases or abnormalities identified by the minimum evaluations (see Investigating Concurrent Extra-Renal Abnormalities and Diseases below).

If proteinuria is of high magnitude, progressive, or nonresponsive to treatment, a more comprehensive diagnostic investigation is warranted[4] (see Box 2).

Consider saving appropriate blood, serum, or urine samples[a] for possible future testing, as recommended in Table 3.

[a]The following are examples of types of samples that might be saved for later needs:
- Whole blood in EDTA (purple top tube), eg, a sample taken before antimicrobial treatment is initiated may be useful for future PCR testing for certain infectious diseases; a DNA test may be available in some predisposed breeds[6,11,12] or may be banked for future study.
- Serum, eg, for paired antibody testing for certain infectious diseases or for auto-antibody testing.
- Urine, eg, for a Bence Jones protein test or for SDS-PAGE testing, to help differentiate glomerular from tubular proteinuria.

Box 2
Additional Diagnostics Recommended for Dogs With Suspected Glomerular Disease Associated with High Magnitude (UPC ≥3.5) or Progressive Proteinuria, Hypertension, Hypoalbuminemia, and/or Azotemia

If any of the above complications exists:
- Complete abdominal ultrasound examination including evaluation of renal and adrenal architecture, presence of effusion, organomegaly, etc.
- Thoracic radiographs (eg, search for infiltration, effusion, etc.)
- Perform a more comprehensive evaluation for infectious diseases (see Searching for Infectious Disease below)

If hypertensive:
- Assess for extrarenal causes of primary or secondary blood pressure elevations. In the absence of hypoalbuminemia and dehydration, hypertension may rarely be the primary cause of proteinuria. Examples of extrarenal causes of hypertension include hyperadrenocorticism, pheochromocytoma, hyperaldosteronism, adverse drug effects, fluid and/or salt overload, etc.
- Consider echocardiography to check for concentric left ventricular hypertrophy

If hypoalbuminemic, azotemic, or both:
- Rule out neoplasia (imaging, possibly lymph node or bone marrow aspirate)
- Rule out concurrent or other causes of hypoalbuminemia, eg, liver disease, gastrointestinal losses, or malnutrition
- Characterize the cause, time course, and stability of identified azotemia as extrarenal (ie, prerenal or postrenal), acute kidney injury, chronic kidney disease, or acute-on-chronic kidney disease. Stage or grade the kidney disease with the appropriate IRIS classification scheme.[13]

Renal biopsy is recommended, especially if the proteinuria is substantial (UPC is ≥3.5), unresponsive to treatment, or progressive despite institution of standard therapy and/or if administration of immunosuppressive drug therapy has been instituted or is contemplated and when the kidney disease is not end-stage. It cannot be overemphasized that experienced personnel at all stages of procuring, preparing, and then interpreting the renal biopsy, not only by light microscopy but also electron microscopy and immunofluorescence, is paramount to get useful information. See Evaluating Renal Biopsy Findings below.

Potentially helpful, investigational, or academic considerations:
- Antithrombin testing
- Thromboelastography
- SDS-PAGE analysis on urine
- DNA banking for future GWAS studies for predisposed breeds

demonstrated minimal or excessive proteinuria. When the magnitude of proteinuria is relatively mild (eg, UPC <2.0), repeated UPC determinations are recommended to verify persistence of the proteinuria and establish the likelihood of an intrinsic glomerular disease.[4] The greater the magnitude of proteinuria, the more certain it becomes that a glomerular disease is present, and, therefore, repeated UPC determinations are unnecessary merely to verify the presence of glomerular disease when the magnitude of proteinuria is large. However, serial assessments of UPC are important to establish a reliable estimate of the dog's prevailing magnitude of proteinuria as a baseline for comparison to subsequent values to evaluate response (s) to treatment. When the magnitude of proteinuria is large, day-to-day variability in the UPC values obtained from a given dog also increases, making it necessary to average the values obtained on several days to obtain a reliable estimate of the dog's prevailing UPC value.[14] As an alternative to determining the UPC on each of several samples and averaging the values, one can just mix equal volumes of the several samples together, and then determine the UPC value for the mixture.[15]

Searching for Infectious Disease

A variety of infectious diseases can cause renal proteinuria in dogs. Infectious agents potentially associated with renal proteinuria[16] are listed in alphabetical order (Appendix 1) with preferred diagnostic testing methods and laboratory noted, when appropriate; otherwise, multiple diagnostic laboratories are suitable (Appendix 2).

The search for infectious diseases must be guided by clinical judgment. Clinicians must be cognizant of the infectious diseases particular to each patient's environs, including where it may have lived or traveled previously, and test accordingly. For instance, in Lyme endemic areas, consensus recommendations (Box 1) would include a SNAP-4DXPlus or similar screening test for heartworm antigen and antibodies against Lyme, *Anaplasma*, and *Ehrlichia* spp., and Leptospirosis antibody testing. Additional recommendations (Box 2) would include testing for other infectious diseases in the area, such as Babesiosis, Bartonellosis, and in cases with acute presentations, Rocky Mountain Spotted Fever.

As many nonclinical, nonproteinuric dogs have natural exposure antibodies toward *Borrelia burgdorferi*, Lyme seropositivity may represent a nonspecific coincidence in some cases and serve merely as a marker for tick and wildlife exposure. In such cases, testing for co-infections often is warranted. Elution studies have proven that the entity called "Lyme nephritis" is associated with Lyme-specific antigen-antibody complexes causing an immune-mediated glomerulonephritis; however, there is no readily available test to prove that a particular individual's proteinuric nephropathy is caused by its Lyme seropositive status. The magnitude of a dog's quantitative C6 antibody value does not predict illness, but is recommended only to rule out Lyme nephritis, if the value is very low, or to use as a baseline for future comparisons after treatment, if the value is elevated.[17]

Leptospirosis is associated primarily with tubular proteinuria rather than glomerular disease; however, evident hypoalbuminemia in these cases may mimic glomerular disease, and thus a diagnosis of Leptospirosis needs to be excluded in endemic areas.[18] Potential cross-reactivity between antibodies against

Leptospira and *Borrelia* spp. may be problematic and require additional specific confirmatory testing.[18]

Investigating Concurrent Extra-Renal Abnormalities and Diseases

Glomerular diseases are often secondary to disease processes primarily located in other organ systems, and appropriate problem-specific investigation of any concurrent extrarenal diseases or abnormalities identified by the minimum evaluations is crucial. The intent is to identify any disease process that might be incriminated as an underlying secondary cause of a glomerulopathy. This is especially important if effective treatment of the primary disease can reduce or stop its provocation of glomerular injury. General categories of conditions promoting secondary glomerular injury are infectious (see Appendix 1) and noninfectious inflammatory or vascular conditions, certain endocrine disorders (particularly hyperadrenocorticism), neoplasia (especially disseminated malignancies), and immune-mediated disorders. As for infectious diseases, the search for underlying diseases with other pathogeneses must be guided by similar clinical judgment and consideration of general diagnostic principles. Clues to the presence of an identifiable underlying disease are usually present among the findings of the minimum evaluations listed above. The rational search strategy is not to "test for everything" but to investigate the evident clues in a focused and problem-specific manner until their consequential potential explanations (ie, diagnoses of underlying diseases) are either ruled out or ruled in. A more vigorous and exhaustive search is appropriate for patients that have more serious complications of their nephropathies (ie, those in Tiers II and III) than those that do not (ie, those in Tier I). Absence of an identifiable underlying disease is a common occurrence, despite exhaustive diagnostic searching, so it frequently is necessary to decide when to stop unproductive searching. For example, performing diagnostic imaging studies (eg, thoracic radiographs, abdominal ultrasound exam) has higher priority for patients in Tiers II and III than in Tier I (see Table 3). In addition, even if the initial search was unproductive and stopped, it is wise to revisit diagnostic efforts from time to time; some conditions (eg, neoplasia) develop new manifestations as they progress and become more readily detected later in their course. Finally, recognition of some concurrent diseases is important to the management strategy of the nephropathy even if they are not truly an underlying cause of the glomerular disease. Examples include dermatologic or gastrointestinal disorders that are managed in part by diets or drugs that might be suboptimum or contraindicated for the nephropathy. Cardiovascular problems might cause or contribute to difficulties in maintaining adequate fluid balance or distribution.

Testing for Immune-Mediated Disorders. Consideration of performing specific tests related to particular immune-mediated disorders occurs in 2 greatly different clinical settings. The first, and most important of these, is when a dog that has renal proteinuria also exhibits concurrent extrarenal clinical signs or laboratory test findings that might be explained by an immune-mediated disease. Examples include fevers of undetermined origin, especially those with a waxing and waning course; lameness or joint swelling that might be attributable to noninfectious (nonerosive or erosive) polyarthritis; anemia accompanied by changes (eg, spherocytes, poikilocytes) suggestive of a hemolytic process; thrombocytopenia; and certain dermatologic lesions. In this setting, performing tests for various autoantibodies (eg, antinuclear antibody [ANA], Coombs', Rheumatoid factor) is part of an appropriately focused and problem-specific investigation of a suspected underlying disease (see above). Diagnoses of immune-mediated diseases typically are based on a weight-of-the-evidence strategy (ie, multiple findings that are compelling only when they are taken together and support one another) rather than on any single finding considered in isolation. And, when such a disease is diagnosed in a dog with a proteinuric nephropathy, the possibility that the glomerular disease actually is part of a multisystemic immune-mediated disorder (eg, systemic lupus erythematosus) becomes highly relevant, both diagnostically and therapeutically. The second setting in which tests for autoantibodies might be considered is when a dog has renal proteinuria but does not exhibit any signs or test abnormalities (besides the proteinuria itself) that might be explained by an immune-mediated disease. In this setting, a positive test result must be interpreted with great caution. Absent grounds for a weight-of-the-evidence diagnosis of an immune-mediated disease affecting some other organ system, the implications of such a finding are uncertain at best. There is no published or anecdotal evidence available to date that indicates that the results of any test for the presence of autoantibodies (eg, ANA, Coombs') discriminate among dogs with proteinuria, but without extrarenal manifestations of a possible immune-mediated disease in any way, that reliably differentiates those that have an immune-complex glomerulonephritis from those that do not.

Evaluating Renal Biopsy Findings

It is of highest priority that the renal biopsy procedure, from collection to in-depth evaluation, should be performed by experienced personnel. Dogs with suspected glomerular disease are likely to benefit the most from a renal biopsy before the disease has progressed to an advanced stage (IRIS CKD Stage IV), because secondary fibrosis and interstitial nephritis may mask the original glomerular disease. Therapeutic intervention at advanced stages is unlikely to ameliorate the clinical features, and the risk of biopsy-associated complications (eg, bleeding) increases. Before the procedure is performed, hypertension needs to be adequately controlled, and coagulation, including platelet number and function, must be adequate as well (discontinue antithrombotics for at least 3 days prior, and evaluate buccal

Table 3. Diagnostic priorities based on canine glomerular disease tier.

	Tier I Uncomplicated Renal Proteinuria			Tier II Renal Proteinuria with Hypoalbuminemia without Azotemia			Tier III Renal Proteinuria with Azotemia		
	Essential	Recommended	Potentially helpful	Essential	Recommended	Potentially helpful	Essential	Recommended	Potentially helpful
Hx, PE, BPM CBC, Chem UA ± culture UPCs[a]	X			X			X		
Investigate "evident" extrarenal disease		(X)			(X)			(X)	
Abdominal ultrasound	[b]	X		X			X		
Chest radiographs	[b]		X		X			X	
Work-up for hypertension	(X)			(X)			(X)		
Work-up for infectious diseases[a]	X			X			X		
Work-up for hypo-albuminemia				X			(X)		
Classify and work-up for azotemia[a]							X		
Renal biopsy[a]		[b]	X		X			X	
AT, TEG, SDS-PAGE, save samples for DNA, etc.			X			X			X

(X) if appropriate; Hx, history; PE, physical examination; BPM, blood pressure measurement; Chem, biochemical profile; UA, urinalysis; AT, antithrombin; TEG, thromboelastography; SDS-PAGE, sodium dodecyl sulfate-agarose gel electrophoresis.

[a]See text.

[b]A small minority of respondents made this recommendation.

mucosal bleeding time and coagulation times, PT/PTT, if there is any concern about adequacy of hemostasis). The renal biopsy findings required to formulate appropriate therapeutic recommendations for dogs with glomerular diseases generally include ultrastructural (ie, transmission electron microscopic, TEM) and immunostaining (ie, immunofluorescence microscopic, IF) observations, as well as light microscopic (LM) observations obtained with specialized techniques including 3 micron thin sections and appropriate special stains.[19] Moreover, the findings must be evaluated and interpreted by experienced veterinary nephropathologists to be of optimal diagnostic utility. Light microscopy alone usually cannot reliably determine whether immune-mediated glomerular disease exists, and decision-making concerning the use of immunosuppressive protocols is hampered. It is essential that renal biopsies of dogs with glomerular disease contain adequate samples of cortex and are properly processed for LM, TEM, and IF evaluations using suitable fixatives or preservatives, and submitted to a pathology laboratory that routinely performs and interprets evaluations of canine kidney specimens. The centers that perform these evaluations typically provide renal biopsy kits that contain the materials and instructions needed to obtain and submit suitable samples; however, for optimum results, the center must be contacted and kits obtained before biopsy samples are obtained. Centers currently available to provide such services include:

International Veterinary Renal Pathology Service, a joint collaboration of Texas A&M and The Ohio State University

For renal biopsy samples: International Veterinary Renal Pathology Service, Department of Veterinary Biosciences, The Ohio State University, Columbus, OH 43210; Contact: Dr Rachel Cianciolo—rachel.cianciolo@cvm.osu.edu.

For SDS-PAGE on urine samples: International Veterinary Renal Pathology Service, Texas A&M University, College Station, TX, USA; Contact: Dr George E. Lees—glees@cvm.tamu.edu.; Dr Mary B. Nabity—mnabity@cvm.tamu.edu.

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Appendix 1: Infectious diseases associated with renal proteinuria

- *Adenovirus* I antigen/antibody—PCR/ELISA
- *Anaplasma* spp. antigen—cytology, PCR
- *Anaplasma phagocytophilum/platys* antibody—in-house SNAP-4DxPlus (IDEXX), AccuPlex4 (Antech); Quant at reference labs
- *Babesia* spp. antigen—cytology, PCR (NCSU)
- *Babesia* canis/gibsoni antibody—IFA
- *Babesia* microti antibody—Protatek
- *Bartonella* spp. antigen—BAPGM culture and PCR at Galaxy Diagnostics
- *Bartonella* spp. antibody—Western blot (National Veterinary Lab), IFA (Galaxy Diagnostics)
- *Borrelia burgdorferi* natural exposure antibody—in-house SNAP-4DxPlus and Lyme C6Quant (IDEXX), AccuPlex4 (Antech), Multiplex (Cornell University), Abaxis Lyme (Abaxis)
- *Borrelia* spp. (relapsing fever group)—whole cell ELISA, IFA
- *Brucellosis* antigen—culture, PCR
- *Brucellosis* antibody—AGID, RSAT, TAT, FA, ELISA
- *Dirofilaria* antigen—in-house SNAP-4DxPlus (IDEXX), Solo Step CH (HESKA), AccuPlex4 (Antech)
- *Ehrlichia* spp. antigen—cytology, PCR
- *Ehrlichia canis/chaffeensis/ewingii* antibody—in-house SNAP-4DxPlus (IDEXX), AccuPlex4 (*E. canis*, Antech), Quant at reference labs
- *Fungal* (systemic) antigen/antibody—cytology, culture, AGID, Blastomyces urine antigen test
- *Hepatozoon* spp. antigen—PCR (Auburn)
- *Leishmaniasis* antigen/antibody—PCR; ELISA, FA, WB
- *Leptospira* spp. antigen—PCR (IDEXX)
- *Leptospira* spp. antibody—State laboratories
- *Mycoplasma* spp. antigen—PCR (IDEXX)
- *Rickettsia rickettsia* (RMSF) antigen—PCR or DFA (on tissue)
- RMSF antibody—IFA, LA
- *Trypanosomiasis*—cytology, PCR, fast dipstick test, FA, RIP

Appendix 2: Laboratories (in alphabetical order)

Antech Diagnostics, www.antechdiagnostics.com
Auburn University Molecular Diagnostics
Department of Pathobiology, College of Veterinary Medicine
252A Greene Hall
Auburn University
Auburn, AL 36849-5519
334-844-2648
www.vetmed.auburn.edu/index.pl/molecular_diagnostics
www.vetmed.auburn.edu/canine_hepatozoonosis
Galaxy Diagnostics
Animal Health Division
2 Davis Drive
Research Triangle Park
Durham, NC 27709
919-354-1055
www.galaxydx.com
HESKA Veterinary Diagnostic Laboratories, www.heska.com
IDEXX Laboratories, www.idexx.com
National Veterinary Laboratory, Inc.
P.O. Box 239
1 Tice Road
Franklin Lakes, NJ 07417
201-891-2992
www.natvetlab.com
NCSU – College of Veterinary Medicine
ATTN: Vector Borne Disease Lab
1051 William Moore Drive
Room 462A
Raleigh, NC 27607
919-513-8279
www.cvm.ncsu.edu/vhc/csds/ticklab.html
Protatek Reference Laboratory
574 East Alamo Drive, Suite 90
Chandler, AZ 85225
480-545-8499
www.protatek.com/RefLab/index.html