

Proteinuria

(Protein in the Urine)

Basics

OVERVIEW

- “Proteinuria” is the medical term for protein in the urine
- Urinary protein is detected by urine dipstick analysis, urinary protein: creatinine ratio (UP:C of 0.4 or higher in cats or 0.5 or higher in dogs), a urinary albumin:creatinine ratio, or a 24-hour urine protein content over 20 mg/kg body weight
- Urinary protein:creatinine ratio (UP:C) of 0.2 up to 0.4 in cats and 0.2 up to 0.5 in dogs is borderline
- “Microalbuminuria” is the abnormal presence of low concentrations of albumin (a type of protein) in the urine; “microalbuminuria” means small amounts of albumin in the urine, and is in the 1–30 mg/dL range; this range is below the limit of detection of standard urine dipsticks used in clinical practice
- Proteinuria can be caused by changes or diseases involving the body, changes involving the kidney itself, or changes after the urine leaves the kidneys (such as inflammation of the bladder [known as “cystitis”])
- The kidney filters the blood and removes various waste products from the body as it produces urine; the kidney is involved in maintaining the normal fluid volume of the body; each kidney is composed of thousands of nephrons (the functional units of the kidney, each consisting of the glomerulus [a tuft of blood capillaries—the “blood filter”] and a series of tubes and ducts, through which the filtered fluid flows, as urine is produced)



GENETICS

- Familial nephropathies (kidney diseases that run in certain families of animals) associated with loss of protein through the glomerulus (a tuft of blood capillaries—the “blood filter”; condition known as “glomerular proteinuria”) have been described in several breeds of dogs; in only a few has the mode of inheritance been established: Samoyed (x-linked), English cocker spaniel (autosomal recessive), bull terrier (autosomal dominant), Dalmatian (autosomal dominant), Bernese mountain dog (suspect autosomal recessive), Brittany spaniel (autosomal recessive); Doberman pinscher, bullmastiff, Newfoundland, rottweiler, Pembroke Welsh corgi, beagle, Chinese shar-pei, English foxhound, soft-coated Wheaten terrier, and others

SIGNALMENT/DESCRIPTION OF PET

Species

- Dogs
- Cats (less common)

Breed Predispositions

- Protein in the urine originating from the glomerulus of the kidney (glomerular proteinuria) may be the initial manifestation of familial (runs in certain families or lines of animals) kidney disease in soft-coated Wheaten

terriers, bull terriers, English cocker spaniels, Dalmatians, Samoyeds, beagles, Bernese mountain dogs, and Chinese shar-peis

Mean Age and Range

- Not established but likely varies with different diseases
- Familial diseases (diseases that run in certain families of animals) associated with protein in the urine (proteinuria)—tend to occur in younger pets
- Acquired (condition that develops sometime later in life/after birth) loss of protein through the glomerulus (a tuft of blood capillaries—the “blood filter”; condition known as “glomerular proteinuria”)—more likely in middle-aged or older pets

Predominant Sex

- Probably varies with different diseases

SIGNS/OBSERVED CHANGES IN THE PET

- Vary with underlying cause and severity of protein in the urine (proteinuria); pets with glomerular proteinuria may show no signs, or have signs relating to the underlying disease
- Weight loss, sluggishness (lethargy), fluid buildup in various tissues (fluid buildup known as “edema”), difficulty breathing (known as “dyspnea”) if they develop clots in the lungs, difficult or painful urination (known as “dysuria”), frequent voiding of small volumes (known as “pollakiuria”), or blood in the urine (known as “hematuria”); possible distended abdomen; ulcers in the oral cavity (if kidneys are failing leading to nitrogen waste buildup in the bloodstream (known as “uremic ulcers”); changes in pulses
- No signs directly attributed to the presence of protein in the urine (proteinuria)

CAUSES

Prerenal Proteinuria

- Protein in the urine originates from changes or disease in the body, before the kidney
- Overload proteinuria—large amounts of low molecular weight plasma proteins in the glomerular filtrate (such as from excessive breakdown of red blood cells [known as “hemolysis”] or destruction of skeletal muscles [known as “rhabdomyolysis”], production of abnormal proteins or Bence-Jones proteins secondary to cancer) overwhelms the ability of the kidneys to resorb the protein

Renal Proteinuria

- Protein in the urine originates from changes or disease in the kidney itself
- Functional proteinuria—strenuous exercise, fever, low body temperature (known as “hypothermia”), seizures, or accumulation of an increased volume of blood in the veins (known as “venous congestion”); poorly documented causes of proteinuria in dogs and cats
- “Glomerulonephritis” is inflammation and accompanying dysfunction of glomeruli (plural of glomerulus) of the kidney; inflammation most commonly is due to the presence of immune complexes in the glomerulus; examples are membranoproliferative glomerulonephritis and proliferative glomerulonephritis
- Glomerular disease of any type (known as “glomerulonephropathy,” such as membranous nephropathy)
- Inherited inflammation of the kidney (known as “hereditary nephritis”)
- A group of conditions of differing cause in which insoluble proteins (amyloid) are deposited outside cells in the kidneys and various other organs, compromising the normal function of the kidney and other organs (condition known as “amyloidosis”)
- Scar tissue involving the blood vessels (capillaries) of the glomerulus (known as “glomerulosclerosis”); scar tissue develops following some type of injury to the glomerulus
- In general, immune-mediated disease results in the highest amount of protein in the urine (severe proteinuria), although dogs with other glomerular diseases also can have severe proteinuria
- Tubular dysfunction resulting in failure of tubular protein reabsorption is associated with mild-to-moderate proteinuria

Post-renal Proteinuria

- Protein in the urine originates from changes or disease after the urine leaves the kidneys
- Bleeding or inflammation of the urinary bladder, urethra (the tube from the bladder to the outside, through which urine flows out of the body), and reproductive organs (such as the vagina, penis, prostate)

RISK FACTORS

- Long-term (chronic) inflammatory disease (such as infectious and immune-mediated disease) and cancer can lead to development of glomerulonephritis or amyloidosis—examples include heartworm, chronic bacterial infection of skin, uterus, or lining of the heart, mast cell or lymphosarcoma cancers, certain hormonal disturbances (such as Cushing’s disease), infections such as bartonellosis, feline immunodeficiency virus (FIV)
- High blood pressure (known as “hypertension”)
- Long-term (chronic) high levels of lipid (a group of compounds that contain fats or oils) in the blood (known as “hyperlipidemia”); for example, as seen in miniature schnauzers
- Multiple myelomas can produce Bence-Jones proteins, which may be found in the urine

Treatment

HEALTH CARE

- Most dogs and cats with protein in their urine (proteinuria) can be managed as outpatients
- Inpatient care may be required during diagnostic evaluation (such as kidney biopsy) or when complications are associated with kidney failure, blood clots or edema

ACTIVITY

- Maintain normal activity if protein in the urine (proteinuria) is the only laboratory abnormality
- Physical therapy and exercise may limit formation or assist in the mobilization of fluid buildup (known as “edema”) in pets with protein in their urine from the glomeruli of the kidney (glomerular proteinuria) and low levels of albumin in their blood (known as “hypoalbuminemia”)—cage confinement should be avoided for these pets

DIET

- If glomerular disease is suspected, feed a diet moderately reduced in protein, reduced in sodium and rich in omega-3 fatty acids
- Feed prescription diets formulated for kidney disease as recommended by the veterinarian

SURGERY

- Kidney biopsy is needed to diagnose the glomerular disease specifically, when an underlying disease cannot be identified or protein in the urine (proteinuria) has persisted for several months following treatment of the underlying disease

Medications

Medications presented in this section are intended to provide general information about possible treatment. The treatment for a particular condition may evolve as medical advances are made; therefore, the medications should not be considered as all inclusive

- Angiotensin-converting enzyme (ACE) inhibitors should be given to dogs, and possibly cats, with protein in their urine from the glomeruli of the kidney (glomerular proteinuria)
- Angiotensin-receptor blockers (ARB) may be added to the treatment if a significant reduction in protein in the urine (proteinuria) is not achieved with use of an ACE inhibitor
- The use of aldosterone antagonists in the management of protein in the urine (proteinuria) needs further investigation, but may be indicated for pets that have increased aldosterone concentrations following treatment with ACE inhibitors or angiotensin receptor blockers
- Medications to control high blood pressure (hypertension), such as amlodipine, may be necessary for pets with protein in their urine and hypertension, in order to control both problems
- Dogs may also be prescribed anti-clotting medication such as low-dose aspirin or clopidogrel
- Antibiotics may be indicated, if infection is the cause of the protein in the urine (proteinuria)

Follow-Up Care

PATIENT MONITORING

- The urine protein:creatinine ratio (UP:C), urinalysis, blood pressure, albumin, creatinine, and potassium will be

monitored 4 times a year to assess progression of glomerular disease and response to treatment, and should be monitored for several months past resolution of any underlying disease

PREVENTIONS AND AVOIDANCE

- Adult dogs and cats should have annual urinalyses, including determination of urine protein; if protein in the urine (proteinuria) is detected, the tests should be repeated in 2–4 weeks
- Dogs or cats with persistent protein in the urine (proteinuria) or low levels of albumin in the urine (microalbuminuria) of glomerular origin should be evaluated more thoroughly for underlying causes of glomerular injury

POSSIBLE COMPLICATIONS

- Fluid buildup (edema)
- Blood clots (known as “thromboembolism”)
- High blood pressure (hypertension)
- Progressive kidney disease
- Poor wound healing
- Death

EXPECTED COURSE AND PROGNOSIS

- Vary with the cause of protein in the urine (proteinuria)
- Post-renal and pre-renal proteinuria should resolve following resolution of inciting causes
- Most diseases associated with renal tubular proteinuria are progressive
- Although glomerular diseases often are progressive, the rate of progression varies and spontaneous remissions have been reported
- Pets with persistent protein in their urine from the glomeruli of the kidney (glomerular proteinuria) may develop kidney tubular damage, resulting in kidney failure and eventual death
- Some dogs die shortly after the initial detection of protein in the urine (proteinuria), while others remain alive for years

Key Points

- Kidney biopsy is needed to diagnose the glomerular disease specifically, when an underlying disease cannot be identified or protein in the urine (proteinuria) has persisted for several months following treatment of the underlying disease
- Some dogs die shortly after the initial detection of protein in the urine (proteinuria), while others remain alive for years