

Proteinuria

Proteinuria is the presence of protein in the urine. Protein can be detected in the urine using a urine dipstick, which is part of a routine urine test or urinalysis. Trace protein in the urine from a dog may be normal if the urine is well concentrated. However, protein in the urine from a cat or in poorly concentrated urine from a dog is always abnormal. Once protein has been detected in the urine, it is important to try and determine the underlying cause and whether any treatment is required.

What are the causes of proteinuria?

The causes of proteinuria are categorised into pre-renal, renal and post-renal.

Pre-renal causes are associated with a problem occurring before the kidneys, usually changes in the blood or blood flow to the kidneys. They may be physiologic (relating to the normal functioning of the body) or pathologic (relating to disease or illness). Physiologic causes include stress, fever, strenuous exercise or seizures, and these normally result in transient proteinuria that does not require specific treatment. Pathological causes are related to the presence of abnormal or excessive proteins in the bloodstream. These include haemoglobin (due to the breakdown of red blood cells), myoglobin (due to the breakdown of muscles) or globulins (due to inflammatory disease or cancers such as multiple myeloma).

Renal causes are associated with problems in the kidneys themselves, usually due to leaky kidneys. The leak may occur at the level glomeruli (the filters of the kidneys) or from the tubules (that refine the urine by rescuing the useful stuff from the urine and dumping the actual waste into the urine).

Causes of renal proteinuria include:

- Acute kidney injury
- Chronic kidney disease
- Glomerular disease
- Drug reactions
- High blood pressure
- Immune-mediated disease
- Inflammatory disease elsewhere in the body like acute pancreatitis
- Infectious disease such as leptospirosis, tick borne infections, leishmania or heartworm
- Endocrine disease like Cushing's disease
- Cancers

Post-renal causes are due to problems after the kidneys i.e. disease of the lower urinary tract or reproductive tract. Examples include urinary tract infections, urinary tract inflammation, urinary tract stones, urinary tract cancers or prostate disease.

How do we identify proteinuria?

Urine dipstick:

- A urine dipstick is a rapid point-of-care diagnostic tool that can assess the urine for the presence of protein amongst other things.
- It is a qualitative test, which means urine is placed on a reagent strip that changes colour in response to the presence of protein. The colour change gives a rough indication of the amount of protein in the urine (trace, 1+, 2+, 3+).
- A urine dipstick is part of a routine urine test (urinalysis).

Urine protein creatinine ratio (UPC):

- This is a quantitative test that measures the exact amount of protein in the urine so we can determine the magnitude of protein loss. This guides treatment and is also used for monitoring.
- It is important that the urine sample is free of inflammation, blood or other contaminants for the test to be accurate so a routine urine test on a fresh urine sample is performed before running a UPC.
- The amount of protein in the urine can vary throughout the day so a single urine sample may over-estimate or under-estimate this value. To overcome this, we use a pooled urine sample to measure the "average" UPC. We will often ask you to collect 3 morning urine samples over 3 consecutive days. Each urine sample should be placed in a separate container and stored in the fridge until the final sample is collected. Then all the samples can be dropped into the practice for testing.

What further tests are required?

Further tests are required to determine the cause of the proteinuria.

These tests may include:

- Urinalysis
 - This test can identify the presence of proteinuria.
 - It also screens for other urine abnormalities including the presence of glucose, ketones, bilirubin, inflammation, infection, crystals or abnormal cells.
 - This allows us to screen for pre-renal, renal and post-renal causes of proteinuria so is often the first test performed as it can guide further testing requirements.
- Blood tests
 - A haematology (blood cell count) and biochemistry (markers relating to organ health and metabolism) test are performed as a general screening test of overall health.
 - This allows us to screen for pre-renal and renal causes of proteinuria.
- Blood pressure measurement
- Testing for infectious diseases
 - This may include a urine culture to screen for a urinary tract infection.
 - Additional tests will depend on your pet's travel history and vaccination history.
- Imaging
 - Chest x-rays and abdominal ultrasound allow screening for inflammatory diseases and cancer.
- Testing for endocrine disease
 - This may include a blood test or urine test.
- Renal biopsy
 - This is the gold standard test for renal proteinuria where glomerular disease is suspected.
 - If must be performed under a general anaesthetic and involves the removal of a small piece of the kidney.
 - This may be performed under ultrasound guidance or through an abdominal surgery.
 - It is a more invasive test, so it is not always performed and needs careful planning but it is the only way to identify certain diseases of the kidney like immune-mediated disease.

How do we treat for renal proteinuria?

1. Reduce the magnitude of proteinuria:
 - a. This requires the use of drugs to reduce the protein loss at the level of the glomeruli.
 - b. Monitoring is required with blood tests and urine tests to confirm the medication is working and ensure there are no unwanted side effects, and to check for disease progression.
 - c. A small stable increase in the kidney markers on a blood test is expected (this proves the medication is working).

2. Minimise the complications of proteinuria:
 - a. Blood clots
 - i. Proteinuria can lead to the loss of a protein called anti-thrombin 3, a natural anticoagulant, that prevents blood clot formation.
 - ii. This means patients with proteinuria are at risk of developing blood clots and need to be given anti-clotting drugs like clopidogrel or rivaroxaban.
 - b. High blood pressure
 - i. A high blood pressure can cause proteinuria, but it can also develop because of proteinuria.
 - ii. High blood pressure needs to be controlled with medication as it can cause further damage to the kidneys, and damage other organs like the brain, eyes and heart.
 - c. Kidney disease
 - i. Kidney disease can cause proteinuria, but it can also develop because of proteinuria.
 - ii. The mainstay for managing kidney disease is through diet modification.
 - iii. A high quality, low protein renal diet is recommended. The goal of these diets is to reduce the amount of protein presented to the kidneys, reducing the ongoing workload and injury to the kidneys.
 - iv. Phosphate binders may be required to bind phosphate in the gut and prevent its absorption into the bloodstream.
 - v. Omega-3 supplementation is also helpful due to its anti-inflammatory and potentially renal protective effects.

3. Treat the underlying cause if known:
 - a. Specific treatments will be required on a case-by-case basis.
 - b. Immunomodulatory drugs are required for immune-mediated disease.

How do we monitor the treatment of proteinuria?

We monitor through blood tests, urine tests and blood pressure assessment. This is performed 7-10 days after starting or adjusting the dose of medication to reduce the magnitude of proteinuria, and every 3 months in a stable patient.

What is the expected outcome for a patient with proteinuria?

The prognosis for a patient with proteinuria is variable. Some patients remain stable for months to years with appropriate treatments, whereas others can rapidly progress despite treatment. Early identification is important because proteinuria itself can damage the kidneys, cause progressive deterioration in your pet's health and potentially shortening their lifespan.

Summary

When proteinuria is identified, we need to determine the cause, assess the severity and decide whether treatment is needed. An investigatory process involves several diagnostic tests. Lifelong treatment and monitoring are often required to prevent disease progression.