



## Clinical Presentation with Proteinuria

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### Summary

Proteinuria represents an important early physical sign of renal diseases. The degree of proteinuria also represents an important prognostic indicator of developing renal failure. It is also an important marker of increased morbidity and mortality in patients with diabetic nephropathy<sup>1</sup>. Therefore, an early detection of proteinuria enables us to make an early diagnosis and intervention of various kidney diseases. We may be able to delay the patients from reaching end stage renal failure which is the most serious complication of various renal diseases.

### Introduction

The normal amount of protein in the urine is lowered than 150mg/day. It composes of 30 to 50 mg of mucoprotein secreted by the Loops of Henle of kidneys. It contains less than 15mg of albumin. The remaining protein is normally filtered and excreted into urine by the glomeruli of kidneys.

Proteinuria usually reflects an increase in the glomerular permeability that allows the 'leakage' of normally non-filtered macromolecules, such as albumin, across the capillary wall into the urine. The increase in permeability can be due to different causes such as structural damage or the loss of the negative charge in the charge barrier of glomeruli.

### Clinical presentation

Patients with renal diseases can present with isolated proteinuria alone, isolated microscopic haematuria alone, or with both proteinuria and haematuria. The patient can be totally asymptomatic when the degree of proteinuria is mild. It usually picks up incidentally by urinalysis with routine health check for insurance or job application. Symptoms may occur when the degree of proteinuria becomes more severe. Patients may notice the presence of bubbles in the urine. The bubbles can be difficult to flush away in the toilet. The patient may experience increased lethargy and swelling in their feet when the degree of proteinuria is heavy. Hypoalbuminaemia and hypocalcaemia may also present.

The transient presence of protein in urine is not uncommon. It presents in about 4% of men and 7% of women. It may be associated with feverish illnesses, stress and vigorous exercises. Single episode of proteinuria may

resolve in subsequent examinations. It is therefore important to recheck the presence of protein in urine in separate occasions when patient first presented with this symptom<sup>2</sup>.

Orthostatic proteinuria is found mainly in adolescents and is less common in patients over 30 years of age. Protein excretion increased when patient is in upright position and returned to normal in supine position. The diagnosis of this condition can be done by separate collections of urine samples during the day (in upright position) for 8 hours and the night (in supine position) for 8 hours. It is a benign condition. The increased protein excretion resolves spontaneously in most cases.

Persistent proteinuria is most commonly seen in conditions of glomerular disorders and occasionally tubular disorders of kidneys. IgA nephropathy; diabetic nephropathy; hypertensive nephrosclerosis; minimal change disease; and membranous nephropathy are the most common glomerular diseases seen in adults. Minimal change disease is most common in children. Persistent proteinuria can also be present in patients with urinary tract diseases and systemic disorders such as congestive heart failure.

The quantity of proteinuria is important. It reflects the severity of the kidney disease and is an important prognostic indicator of the survival of kidney in patients with IgA nephropathy and diabetic nephropathy<sup>3</sup>. It enables doctors to identify those patients at higher risk of developing renal failure in the future. The continuous monitoring of the quantity of proteinuria is also important to guide the adjustment of treatment. An accurate documentation of degree of proteinuria is most useful. It should be done by the measurement with a 24-hours urine collection whenever possible.

### Investigation

Urine dipstick analysis primarily detects albumin for protein. However, it can be a relatively insensitive test. It usually gives a false negative result when the total urine protein excretion is below 300-500mg/day. Urine protein concentration can also be easily influenced by the variation of urine volume. A false positive result can be given in patients with recent contrast medium administration (e.g. IVU). However, it can be a very handy and useful tool for a continuous monitoring of the progress of the kidney disease at a busy clinic. It is possible to reduce the



effect of variation of urine volume in the urine protein concentration by calculating the total protein-to-creatinine ratio (mg/mg) on a random urine specimen. The drawback is the ratio can be affected by variations in body size and the state of nutrition of patients.

Analysis of the type of protein can also be useful in making the diagnosis. Highly selective of small size protein molecules in urine is commonly found in patients with minimal change disease of kidney. The high level of Bence Jones protein is found in patients with multiple myeloma. Microscopic study of urine for dysmorphic red blood cells and sediments with cellular or hyaline casts usually indicate glomerular diseases of the kidney. MSU should be sent for bacterial culture. IVU and ultrasound study of kidneys are also important tests to identify other pathological causes. Creatinine clearance should also be measured. Renal biopsy should be considered when the patient presents with heavy proteinuria, and continue worsening of proteinuria and/or renal function despite treatment. Blood pressure control is most important with the target of 130/80mmHg with stable renal function and 125/75mmHg with progressive proteinuria.

### Conclusions

The evaluation of mild proteinuria should begin with testing the urine on at least two separate occasions. The urine sediment should also be examined and looked for

other signs of glomerular disease such as haematuria and red cell casts. Persistent proteinuria should be evaluated with a 24-hour urine collection. The 24-hour collection should be split into upright and supine specimens in adolescents and young adults in whom orthostatic proteinuria may be a consideration.

A careful history is also required especially with systemic diseases such as hypertension, diabetes mellitus, and congestive heart failure.

If the proteinuria persists and the history is not helpful, a renal ultrasound or IVU should be considered to look for a structural lesion such as polycystic kidney disease or chronic pyelonephritis. Periodic monitoring of proteinuria with a 24-hour urine collection is indicated when the above evaluations are negative, the urine sediment is benign, and the blood pressure and plasma creatinine concentration are normal. A renal biopsy is generally performed in this setting when there are some signs of progressive disease such as a rising protein excretion or the plasma creatinine concentration or worsening CrCl.

### References:

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2. Larson T: Evaluation of proteinuria. *Mayo Clin Proc* 69:1154, 1994.
3. Suzuki S, Joh K. Applicability of steroid therapy in 275 adult patients with IgA nephropathy determined using a histological scoring system and degree of proteinuria. *Clin Exp Nephrol.* 2004 Jun;8(2):109-16.

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