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Key words

Glomerulonephritis; interstitial nephritis; nephrotic syndrome; proteinuria; postural proteinuria

Abstract

Proteinuria is a common laboratory finding in children. It might represent a benign condition or herald the presence of a serious underlying renal disease or systemic disorder. Investigation to confirm a diagnosis or seek reassurance is important. This paper discusses the various causes of proteinuria, and those aspects of the history, physical examination, and the laboratory tests that will help determine the cause or reassure that a serious problem is not currently present.

Proteinuria is defined as the excretion of an excessive amount of protein in the urine (Robson and Leung, 1991). The upper limit of acceptable protein excretion in a 24-hour urine collection varies by age and is shown in Table 1. The major protein components of normal urine in children are Tamm-Horsfall protein (50%), albumin (20%), IgG (10%) and light chains (7%). Severe proteinuria is defined as greater than 1 g of protein in the urine per 24 hours or a random urine protein to creatinine ratio (U Pr/Cr mg/mg) greater than 1.0. Nephrotic range proteinuria is defined as proteinuria >40 mg/m^2/hr (Report of a Workshop by the British Association for Paediatric Nephrology and Research Unit, Royal College of Physicians, 1994).

Measurement of proteinuria

Qualitative methods

The urine dipstick test (Albustix) is based on the tetrabromophenol blue colorimetric test and is the most widely used screening test (Harrison *et al*, 1989). The intensity of colour change from yellow to blue is correlated to the amount of protein in the urine and is expressed from the colour chart with various shades of blue as trace (10 mg/dL), 1+ (30 mg/dL), 2+ (100 mg/dL), 3+ (300 mg/dL) and 4+ (≥1000 mg/dL) (Loghman-Adham, 1998). In the absence of protein, the dipstick will remain yellow. Only 1+ or more is considered abnormal. The dipstick test primarily detects albuminuria and is not sensitive for low molecular weight proteins, gamma globulins, haemoglobin and Bence Jones proteins (Robson and Leung, 1991). The causes of false positive and false negative results are shown in Table 2. The most common limitation is the effect of urine concentration on trace and 1+ dipstick protein results. A dilute urine with a specific gravity <1.010 can result in a false negative trace dipstick result; conversely, a concentrated urine with a specific gravity >1.030 can result in a false positive 1+ dipstick result. This limitation has a significant impact on the interpretation of screening tests. The sensitivity of the dipstick test is only 70% and the specificity only 68% (Abitol *et al*, 1990).

The turbidometric test, which uses sulphosalicylic acid as a precipitating agent, detects all forms of protein. In this method, three drops of a 20% solution of sulphosalicylic acid are added to 5 mL of urine. Depending on the amount of protein precipitated, various grades of turbidity from minimal (trace) to heavy flocculation (4+) are noted (Makker, 1992). The turbidometric method also has limitations (Table 3). Urine with a specific gravity greater than 1.015 is necessary for reliable results (Loghman-Adham, 1998). The turbidometric test is generally used as a supplementary test when there is suspicion of the presence of a low molecular weight or other protein which is not detected by the dipstick method.

TABLE 1

Normal urinary protein excretion by age

Age	Normal limit of urinary protein mg/day
2-12 months	155
1-4 years	140
5-10 years	190
11-16 years	250

Adapted from Norman (1987).

Quantitative methods

The 24-hour quantitative urine protein excretion, the gold standard against which other tests are compared, is not practical in children who are incontinent. The test also has an inherent time delay, is often difficult to obtain in an outpatient setting, and is subject to collection errors (Robson and Leung, 1991). The random U Pr/Cr is a convenient method for estimating urine protein excretion without a 24-hour urine collection (Kristal *et al*, 1988; Abitol *et al*, 1990). The total protein (gm/m²/day) in the urine can be estimated using the equation 0.63 U Pr/Cr (Abitol *et al*, 1990). Because serum and urinary creatinine are dependent on muscle mass, this technique is not valid in children with severe malnutrition or high lean body mass. In the presence of a significant reduction in the glomerular filtration rate, tubular secretion of creatinine increases, and this might result in an artifically low U Pr/Cr ratio (Loghman-Adham, 1998). The U Pr/Cr ratio is especially useful to follow trends in proteinuria and in this situation a first morning urine is optimal since this excludes any postural effect on the protein component of the ratio.

Epidemiology

Proteinuria is found during routine urine testing in up to 10% of schoolchildren (Randolph *et al* 1967; Vehaskari *et al*, 1982); repeat testing reduces this figure to 0.1% (Randolph *et al* 1967; Wagner *et al*, 1968; Dodge *et al* 1976; Vehaskari *et al*, 1982). In a study of 8,954 schoolchildren, proteinuria was documented in at least one of four specimens in 10.7%, two specimens in 2.5%, and all four specimens in only 0.1% of the children (Vehaskari and Rapola, 1982).

The prevalence of proteinuria increases with age, peaks during adolescence and is more common in girls (Randolph *et al*, 1967; Wagner *et al*, 1968; Dodge *et al*, 1976; Vehaskari and Robson, 1994).

Pathophysiology

The glomerular capillary wall contains a proximal electrostatic barrier and a distal size selective barrier (Myers and Guasch, 1994). The electrostatic barrier consists of negatively charged sialoproteins and proteoglycans, such as heparan sulfate (Watson, 1998). Most proteins are too large or have a charge or conformation that renders them unable to traverse the small charged pores in the lamina densa of the basement membrane or the slit pores between the foot processes of the epithelial cells of the glomerulus. Molecules with a radius of less than 20Å freely pass the glomerular basement membrane, while passage is restricted for those with radius greater than 45-50Å. Albumin has a radius of 36Å and is moderately restricted by size (Ettenger, 1994). The majority of protein that is filtered at the glomerulus is reabsorbed in the proximal tubule.

Proteinuria might result from increased glomerular permeability due to loss of the negative charges in the basement membrane, or an increase in the effective pore size or number of pores as a result of damage to the basement membrane (Watson, 1998). Haemodynamic alterations in glomerular blood flow secondary to a reduced number of functioning nephrons - or to the effects of angiotension II or other vasoactive amines, can result in proteinuria due to increased diffusion of protein across the glomerular basement membrane (Watson, 1998).

Tubular proteinuria occurs when there is an increased excretion of the normally filtered low molecular weight proteins (<40,000 daltons) such as β_2-microglobulin, α_1-microglobulin, retinol-binding protein and lysozyme - or damage to the tubules with release of high molecular weight lysosomal enzymes such as alanine aminopeptidase and N-acetyl-ß-D-glucosaminidase. Retinol-binding protien and N-acetyl-ß-glucosaminidase are the preferred measurements and these tests are emerging as markers of subtle or early renal injury. Although currently of limited clinical usefulness, these tests are likely to find a role in the routine assessment of renal problems.

Glomerular proteinuria might be selective or nonselective. Proteinuria is considered 'selective' when the glomerular capillary wall leaks predominantly small molecular weight proteins such as albumin (molecular weight: 69,000 daltons) and 'nonselective' when there is also leakage of large molecular weight proteins (Makker, 1992). The selectivity proteinuria index (SPI) can be measured by determining the clearance ratio of IgG (molecular weight 160,000 daltons) to albumin. An SPI of >0.1 denotes nonselective proteinuria.

Aetiology

The causes of proteinuria in children are listed in Table 4.

Functional or haemodynamic proteinuria

Functional proteinuria is usually transient and clears when the inciting factor remits or is removed. It is likely that the functional proteinuria seen with cold exposure, congestive heart failure, and epinephrine administration is due to haemodynamic alterations in glomerular blood flow (Vehaskari and Robson, 1992; Ettenger, 1994).

Overflow proteinuria

Overflow proteinuria occurs when the plasma concentrations of small molecular

TABLE 2

Causes of false positive and false negative results with the dipstick test for proteinuria

False positive results	False negative results
Highly concentrated urine (SG>1.030) Alkaline urine (pH>8) Gross haematuria Pyuria Bacteriuria Prolonged immersion Placing reagent strip directly in the urine stream Quaternary ammonium compounds and detergents Phenazopyridine	Very dilute urine (SG<1.010) Acidic urine (pH<4.5) Low molecular weight proteinuria

Modified from Robson and Vehaskari (1994).

TABLE 3

Causes of false positive and false negative results with sulphosalicyclic acid test for proteinuria

False positive results	False negative results
Highly concentrated urine (SG>1.030) Gross haematuria Pyuria Bacteriuria Radiographic contrast media High levels of cephalosporins, penicillins, or penicillin analogues Metabolites of tolbutamide and sulphonamides	Very dilute urine (SG<1.010)

Modified from Robson and Vehaskari (1994).

weight proteins exceed the capacity of the tubules to reabsorb the filtered protein (Loghman-Adham, 1998). Examples include albuminuria with excessive transfusion of albumin, haemoglobinuria in intravascular haemolysis, and myoglobinuria in rhabdomyolysis (Leung and Robson, 1987).

Orthostatic proteinuria

Orthostatic proteinuria accounts for up to 60% of all cases of asymptomatic proteinuria in childhood, and the incidence is highest in adolescence. The diagnosis is suggested by finding normal protein excretion in the supine posture and increased protein excretion in the upright position. Orthostatic proteinuria is presumed to be due to changes in renal blood flow that occur with the erect posture or mild glomerular changes of unknown etiology (Vehaskari, 1990). Left renal vein entrapment might be responsible for some cases of orthostatic proteinuria (Shintaku *et al*, 1990). In young adults, follow-up for as long as 50 years suggests a benign prognosis (Glassock 1981; Rystand and Spreiter, 1981).

Glomerular diseases

Glomerular causes include the various causes of glomerulopathy and nephrotic syndrome. The various causes of glomerulopathy are shown in Table 5. Nephrotic syndrome is characterized by oedema, hypoalbuminaemia (<25 g/L), hyperlipidaemia, and proteinuria >40 mg/m²/h (Report of a Workshop by the British Association for Paediatric Nephrology and Research Unit, Royal College of Physicians, 1994). Nephrotic syndrome associated with primary glomerular disease is termed primary nephrotic syndrome and is classified according to the histologic findings shown in Table 6. Secondary nephrotic syndrome occurs due to glomerulopathy associated with a systemic disease.

Proteinuria associated with minimal change nephrotic syndrome is due to both a size and charge selective mechanism (Myers and Guasch, 1994). Glomerulonephritis results in an increase in glomerular pore size consequent upon damage upon the glomerular basement membrane.

Interstitial nephritis

Interstitial nephritis includes a variety of pathological processes that participate in the progression of most renal diseases and is a final common pathway for all forms of end stage renal disease (Neilson 1989; Jones and Eddy, 1992). Interstitial nephritis might be a primary disease or secondary to a variety of renal problems. The causes of interstitial nephritis are shown in Table 4. In most cases, the cause is unknown. An immunopathophysiology is likely to be operative in the majority. The diagnosis is often not made until renal biopsy. Interstitial nephritis is the final diagnosis in 5 to 7% of renal biopsy specimens obtained for any reason and accounts for 2% of acute renal failure in children (Jones and Eddy, 1992).

Renal tubular disorders

Tubular proteinuria is found in a variety of inherited or acquired disorders and might be associated with other defects of proximal tubular function, such as glycosuria, phosphaturia, and uricosuria. In general, the proteinuria associated with renal tubular disorders is mild and rarely exceeds 1 g/24 h. Tubular proteinuria rarely presents a diagnostic dilemma because the underlying disease is usually detected before the proteinuria (Bergstein, 1996).

Clinical evaluation

A thorough history and a complete physical examination are important in the evaluation of proteinuria.

History.

Age of onset

The younger the child, the more likely that a significant cause will be found. Proteinuria seen in the first few months of life suggests a congenital cause such as congenital nephrotic syndrome or a primary renal tubular disorder. Orthostatic proteinuria occurs later in childhood with a peak incidence in adolescence.

Severity

Orthostatic and tubular proteinuria are usually less than 1 g/24 h whereas glomerular proteinuria is usually greater than 1 g/24 h.

Associated symptoms

Asymptomatic proteinuria usually originates in the kidney. Urethral dysuria associated with mild proteinuria suggests an inflammatory or irritative problem in either the urethra or bladder. Suprapubic discomfort suggests a problem in the bladder. Flank or unilateral low back pain suggests a problem in the kidney.

Discomfort with voiding, frequency, incontinence, and cloudy, foul smelling urine are common associated symptoms when the proteinuria is due to urinary tract infection (Leung and Robson, 1991). A seropurulent urethral discharge might be present in urethritis.

Haemoptysis suggests the possibility of Goodpasture's syndrome, Wegener's granulomatosis, or tuberculosis. Unexplained bruising in the lower extremities, arthritis, abdominal pain or testicular swelling and discomfort suggest the diagnosis of Henoch Schönlein purpura. Bloody diarrhoea suggests the possibility of haemolytic uremic syndrome (Robson *et al*, 1993). Symptoms of arthritis, Raynaud's phenomenon, alopecia, photosensitivity, weight loss, and malar rash suggest a collagen vascular disease, such as systemic lupus erythematosus (Robson and Leung, 1991).

TABLE 4

Causes of proteinuria

- **A. Functional proteinuria**
  - 1. Cold exposure
  - 2. Congestive heart failure
  - 3. Epinephrine administration
- **B. Overflow proteinuria**
  - 1. Excessive albumin transfusion
  - 2. Intravascular haemolysis
  - 3. Rhabdomyolysis
- **C. Orthostatic proteinuria**
- **D. Glomerular diseases**
  - 1. Nephrotic syndrome
  - 2. Glomerulonephritis
- **E. Interstitial nephritis**
  - 1. Primary or isolated
    - a. Infection
    - b. Drug exposure
    - c. Immunological disease
    - d. Idiopathic
  - 2. Associated with primary glomerulonephritis
  - 3. Associated with structural renal disease
    - a. Vesicoureteric reflux
    - b. Obstruction
    - c. Cystic disease
  - 4. Hereditary and metabolic
    - a. Familial nephronophthisis
    - b. Idiopathic familial interstitial nephritis
    - c. Cystinosis
    - d. Wilson syndrome
    - e. Sickle cell disease
    - f. Hypercalcaemia
    - g. Hyperuricaemia, Lesch-Nyhan syndrome
    - h. Hyperoxaluria
    - i. Hypokalaemia
  - 5. Neoplastic disease
  - 6. Miscellaneous
    - a. Allograft rejection
    - b. Heavy metals (cadmium, lead, mercury)
    - c. Radiation
    - d. Balkan nephropathy
    - e. Idiopathic
  - 7. Associated with chronic progressive renal disease of any aetiology
- **F. Renal tubular disorders**
  - 1. Primary renal tubular disorders
    - a. Isolated tubular proteinuria
    - b. Fanconi syndrome (primary and secondary causes)
  - 2. Tubular toxins
    - a. Drugs (aminoglycosides, penicillin, polymyxins, cephalosporin, phenacetin, naproxen, allopurinol, phenindione)
    - b. Heavy metals (mercury, gold, lead, bismuth, copper)
  - 3. Ischaemic tubular injury
  - 4. Miscellaneous
    - a. Reflux nephropathy
    - b. Polycystic kidney disease
    - c. Renal transplant rejection

Past health

A history of recurrent pyelonephritis or unexplained fever in infancy might be a clue to the presence of a scarred kidney. Proteinuria that occurs several weeks after an infection with group A ß-haemolytic streptococci is suggestive of post-streptococcal glomerulonephritis. A history of an episode of streptococcal tonsillitis, scarlet fever, or impetigo in the preceding year might be a clue to the presence of an unrecognized episode of post-streptococcal glomerulonephritis (Robson and Leung, 1992). A history of hepatitis suggests the possibility of membranous glomerulonephritis secondary to hepatitis B. A child with a past history of tuberculosis might have renal tuberculosis. A history of infectious mononucleosis, or other viral infection suggests the possibility of a viral post-infectious glomerulonephritis. A history of blood transfusion might be a clue to the presence of focal glomerulosclerosis due to acquired immunodeficiency syndrome or glomerulopathy due to infection with hepatitis B or C. Proteinuria that occurs intermittently with macroscopic haematuria and coincidentally with upper respiratory or other intercurrent infection is common with IgA nephropathy, hereditary nephritis, thin membrane disease, and membranoproliferative glomerulonephritis (Robson and Leung, 1991).

TABLE 5

Aetiologic classification of glomerulopathy in childhood

1. **Postinfectious**
   a. Group A ß-haemolytic *Streptococcus*
   b. Viral infection (varicella, hepatitis B and C, human immunodeficiency virus type 1, infectious mononucleosis)
   c. Subacute bacterial endocarditis
   d. Syphilis
   e. Malaria
   f. Tuberculosis
2. **IgA nephopathy**
3. **Hereditary**
   a. Hereditary nephritis
   b. Thin membrane disease
4. **Vasculitis**
   a. Henoch Schönlein purpura
   b. Systemic lupus erythematosus
   c. Polyarteritis nodosa
   d. Wegener granulomatosus
5. **Sickle cell disease**
6. **Goodpasture syndrome**
7. **Diabetes mellitus**
8. **Amyloidosis**
9. **Malignancy** (leukemia, lymphoma, Wilms tumor, pheochromocytoma)
10. **Toxins** (bee sting, poison ivy, snake venom)
11. **Renal vein thrombosis**
12. **Medications** (probenecid, fenoprofen, captopril, lithium, warfarin, penicillamine, mercury, gold, trimethadione)
13. **Heroin**
14. **Idiopathic**

A history of right-sided heart failure or pericarditis might suggest a renal vein congestion syndrome. Renal vein thrombosis is more common in infants of diabetic mothers, children with nephrotic syndrome, or children with severe dehydration. A history of congenital heart disease suggests the possibility of a proliferative glomerulonephritis associated with subacute bacterial endocarditis.

A child with rheumatoid arthritis might develop proteinuria due to glomerulonephritis, amyloidosis, or treatment with gold or anti-inflammatory medications.

Foreign travel

A history of foreign travel and contact with a specific infectious agent might be important. A child who has proteinuria after a trip to a region endemic for malaria might have glomerulonephritis due to malaria.

Drug use

A complete drug history should be obtained, since medications might be associated with proteinuria (Table 3 and Table 4).

Family history

Attention should be paid to any evidence of deafness or visual disorders, which might suggest hereditary nephritis (Robson and Leung, 1991). A family history of hereditary nephritis, thin membrane disease, polycystic kidney disease or a renal tubular disorder suggests the corresponding illness.

Physical examination

General

Weight, height, and head circumference should be plotted on standard growth charts. Growth failure might occur in children with reflux nephropathy, chronic renal failure of any cause, and tubular disorders associated with renal tubular acidosis (Robson and Leung, 1991).

Vital signs such as blood pressure and heart rate should be noted. Hypertension is common in renal disease.

Associated signs

Periorbital, presacral, genital, and ankle oedema are common in children with nephrotic syndrome. Polythelia (Leung and Robson, 1989a), a preauricular sinus (Leung and Robson, 1992), a single umbilical artery (Leung and Robson, 1989b), and low set or malformed ears, all suggest the possibility of a congenital urinary problem such as hydronephrosis or a cystic or dysplastic kidney.

Deafness or visual impairment suggests hereditary nephritis. Dependent or pressure-sensitive petechiae or purpura, arthritis, or testicular swelling and tenderness suggests Henoch Schönlein purpura. A malar rash, Raynaud's phenomenon, alopecia, or arthritis suggests collagen vascular disease such as systemic lupus erythematosus. A vasculitic rash might be present in Wegener's granulomatosis.

Enlarged kidneys suggest the possibility of polycystic kidneys or hydronephrosis. Loin tenderness suggests an inflammatory lesion in the kidneys such as pyelonephritis. A large bladder suggests urethral obstruction. Suprapubic tenderness suggests an inflammatory lesion in the bladder such as cystitis.

Ascites and pleural effusion suggest nephrotic syndrome. Pulmonary oedema and congestive heart failure might be part of an acute nephritic presentation.

Laboratory investigations

In addition to confirming the presence of proteinuria, a first morning urinalysis might give a clue to the aetiology. To assess the possibility of orthostatic proteinuria, the bladder should be emptied in the evening before bed and the urine should be obtained immediately upon rising. If the concentration of protein is not greater than a trace (10 mg/dL) in the first morning specimen but 1+ (30 mg/dL) or greater amounts are found later in the day, the diagnosis of orthostatic proteinuria can be established. We request a minimum of 7 twice a day home urine tests to assess for orthostatic proteinuria.

In the microscopic examination, the urine should be examined as fresh as possible to minimize the possibility of the lysis of red and white blood cells. The specimen should not be refrigerated prior to microscopic analysis, since this will cause precipitation of solutes that will obscure the analysis. Tea- or coke-coloured, brown, dark-green, or black urine suggests a lesion in the kidney or intravascular haemolysis. Pink and bright-red urine, particularly when clots are visible, usually indicates a lesion in the urethra or bladder. Floating debris may represent fragments from a stone, or collections of purulent material, or uroepithelial tissue. The presence of white blood cells suggests an inflammatory lesion. Eosinophils might be present in interstitial nephritis and can be demonstrated with Wright's stain. White blood cell casts suggest interstitial nephritis. Red blood cell casts suggest glomerulonephritis. A significant percentage of dysmorphic red blood cells observed by phase contrast microscopy suggests glomerulonephritis. The presence of lipid bodies and lipid casts suggests

TABLE 6

Histologic classification of glomerular lesions associated with primary nephrotic syndrome

A. Minimal change nephrotic syndrome
B. Diffuse mesangial hypercellularity
C. Focal glomerulosclerosis
D. Membranous glomerulonephritis
E. Membranoproliferative glomerulonephritis

Adapted from Robson and Leung (1993)

nephrotic syndrome. Microscopic bacteriuria are suggestive, but not diagnostic, of urinary tract infection (Leung and Robson, 1991). Infection should be confirmed with culture of an appropriately obtained urine specimen (Leung and Robson, 1991). Glucosuria might be a clue to a tubular disorder.

Proteinuria greater than 1g/24 h usually indicates a glomerular lesion. The relative permeability of the glomerular filter to protein of various molecular sizes correlates with the type and severity of glomerular disease on biopsy (Ghiggeri, 1988). Patients with minimal change nephrotic syndrome have selective proteinuria and a SPI less than 0.1, whereas those with more severe histologic varieties of nephrotic syndrome have non-selective proteinuria and a value greater than 0.1.

Low molecular weight proteinuria usually originates from tubular loss of protein. In contrast, glomerular injury results in loss of small molecular weight protein such as albumin.

The detection of retinol-binding protein, and N-acetyl-ß-D-glucosaminidase in the urine are reliable non-invasive methods to diagnose proximal tubular disorders or damage (Portman *et al*, 1986).

The presence of protein in the urine of the parent or sibling might be a clue to an inherited problem, such as hereditary nephritis, thin membrane disease, polycystic kidney disease or a renal tubular disorder.

A complete blood count, erythrocyte sedimentation rate, and serum urea and creatinine should be obtained routinely. The presence of anaemia suggests sickle cell disease or a chronic renal problem. An elevated erythrocyte sedimentation rate or leukocytosis suggests an inflammatory problem. An elevation in serum urea or creatinine suggests a renal parenchymal problem with a decrease in glomerular filtration rate.

Other tests should be ordered when indicated by history, physical examination, or initial laboratory results. A C_3 should be ordered if there is evidence for glomerulonephritis. The causes of hypocomplementaemic glomerulonephritis include post-infectious glomerulonephritis, membranoproliferative glomerulonephritis and systemic lupus erythematosus. An antistreptolysin O (ASOT) titre should be ordered if post-streptococcal glomerulonephritis is suspected. Anti-hyaluronidase and anti-deoxyribonuclease B titres should be considered if the ASOT is normal but the suspicion for post-streptoccal glomerulonephritis is high. An anti-nuclear factor or double stranded anti-DNA antibody titre should be ordered if a collagen vascular disease is suspected. A depressed serum total protein and albumin together with an elevated serum cholesterol suggest nephrotic syndrome. An anti-neutrophil cytoplasmic antibody test should be obtained if there is suspicion of Wegener's granulomatosis or polyarteritis nodosa. A hyperchloraemic metabolic acidosis with a normal anion gap suggests renal tubular acidosis, which might be present in tubular disorders, obstruction, and interstitial nephritis.

Diagnostic imaging studies

An ultrasound of the urinary tract with Doppler analysis of the renal veins is an appropriate non-invasive screening test for anatomical abnormalities. Cysts, areas of acute or chronic pyelonephritis, obstruction, diffuse renal parenchymal disorders, and evidence of renal vein compression or renal vein thrombosis are detectable by ultrasound and Doppler analysis. An intravenous pyelogram is no longer indicated in the routine investigation of a child with proteinuria. If small or scarred kidneys are present on the ultrasound or if the history suggests pyelonephritis, a retrograde voiding cystourethrogram should be considered in order to look for vesicoureteric reflux. A dimercaptosuccinic acid (DMSA) scan is the preferred study to detect renal scars. A chest X-ray might reveal pulmonary infiltrates in Goodpasture's syndrome or Wegener's granulomatosis, pleural effusion in nephrotic syndrome or congestive heart failure, and pulmonary oedema in acute glomerulonephritis.

Renal biopsy

A renal biopsy is not routinely indicated for the investigation of a child with proteinuria. A biopsy should be considered when proteinuria is accompanied by haematuria, hypertension, a persistently low serum complement, a persistently depressed glomerular filtration rate, signs or symptoms suggestive of collagen vascular disease, chronic renal failure of unknown etiology, or a positive family history of chronic renal disease (Robson and Leung, 1991). A renal biopsy should be considered in selected cases of nephrotic syndrome associated with a later age of onset, nonselective proteinuria, or unresponsiveness to treatment with a corticosteroid medication. Proteinuria unassociated with any of the above clinical situations but that persists for more than one year is unlikely to resolve and some authors recommend a renal biopsy to clarify the histologic diagnosis (Yoshikawa *et al*, 1991; Trachtman *et al*, 1994).

Management

The treatment of proteinuria should be directed to the underlying cause. When no aetiology can be identified, the parents and child may be reassured if the child has asymptomatic proteinuria, no associated haematuria, and a normal blood pressure, glomerular filtration rate, and renal ultrasound. Regular follow-up, however, is

important as long as significant proteinuria persists. A child with persistent proteinuria should be checked every 6 to 12 months with a physical examination, including blood pressure, urinalysis, and blood tests for creatinine and urea. Physical activity should not be restricted. A referral to a paediatric nephrologist should be considered in any child with severe proteinuria, oedema, macroscopic haematuria, hypertension, active urine sediment with casts, low glomerular filtration rate or parental anxiety.

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