Nefrologia pediatrica tra aggiornamento e linee guida
Sabato 14 novembre 2015
Università degli Studi di Milano-Bicocca, Monza

Ematuria e proteinuria

Giovanni Montini
Milano, Italy

giovanni.montini@unimi.it
“The heart beats, the lung breathes—the kidney does not make any noise, and often people end up presenting with end-stage kidney disease having never realised anything was wrong.”

G. Remuzzi, *The Lancet* 2010
1.783,000 adult patients are treated either with dialysis or have received a kidney transplant. There is an annual increase of 5-8%
Global impact of kidney disease

- Chronic Kidney disease has been recognised as a major public health burden

- Population prevalence of CKD >10%

- Recognition of the burden of chronic kidney disease, its risk factors, and implementation of prevention strategies is, therefore, key to saving many lives

Eckardt, Lancet 2013
A nationwide study of mass urine screening tests on Korean school children and implications for chronic kidney disease management

Byoung-Soo Cho · Won-Ho Hahn · Hae Il Cheong · Inseok Lim · Cheol Woo Ko · Su-Young Kim · Dae-Yeol Lee · Tae-Sun Ha · Jin-Soon Suh

Published online: 08 November 2012

Materials and methods

Between 1999 and 2008, 47,057,545 school children, including 25,913,563 elementary school children (6–11 years old); 12,335,213 middle school children (12–14 years old); and 8,808,769 high school children (15–17 years old) participated in a mass school urine screening program in Korea.
Table 1  Demographic findings of school children participating in the Korean mass urine screening

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>N (% of subjects)</th>
<th>Age (years) (mean ± SD)</th>
<th>Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>N (% of each group)</td>
</tr>
<tr>
<td>IH</td>
<td>3,724 (72.82)</td>
<td>9.85 ± 2.82</td>
<td>997 (26.77)</td>
</tr>
<tr>
<td>IP</td>
<td>552 (10.79)</td>
<td>12.00 ± 2.47</td>
<td>52 (9.09)</td>
</tr>
<tr>
<td>CHP</td>
<td>838 (16.39)</td>
<td>10.63 ± 3.41</td>
<td>429 (51.19)</td>
</tr>
<tr>
<td>Total</td>
<td>5,114 (100)</td>
<td>10.16 ± 2.94</td>
<td>1,478 (28.79)</td>
</tr>
</tbody>
</table>

IH isolated hematuria, IP isolated proteinuria, CHP combined hematuria and proteinuria,
<table>
<thead>
<tr>
<th>Subgroup</th>
<th>N (% of subjects)</th>
<th>Age (years) (mean ± SD)</th>
<th>Biopsy N (% of each group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IH</td>
<td>3,724 (72.82)</td>
<td>9.85 ± 2.82</td>
<td>997 (26.77)</td>
</tr>
<tr>
<td>IP</td>
<td>552 (10.79)</td>
<td>12.00 ± 2.47</td>
<td>52 (9.09)</td>
</tr>
<tr>
<td>CHP</td>
<td>838 (16.39)</td>
<td>10.63 ± 3.41</td>
<td>429 (51.19)</td>
</tr>
<tr>
<td>Total</td>
<td>5,114 (100)</td>
<td>10.16 ± 2.94</td>
<td>1,478 (28.79)</td>
</tr>
</tbody>
</table>

*IH* isolated hematuria, *IP* isolated proteinuria, *CHP* combined hematuria and proteinuria,
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunoglobulin A nephropathy</td>
<td>576</td>
<td>38.97</td>
</tr>
<tr>
<td>Mesangial proliferative glomerulonephritis (GN)</td>
<td>359</td>
<td>24.29</td>
</tr>
<tr>
<td>Thin basement membrane disease</td>
<td>194</td>
<td>13.13</td>
</tr>
<tr>
<td>Henoch–Schönlein purpura nephritis</td>
<td>30</td>
<td>2.03</td>
</tr>
<tr>
<td>Membranoproliferative GN</td>
<td>25</td>
<td>1.69</td>
</tr>
<tr>
<td>Membranous GN</td>
<td>21</td>
<td>1.42</td>
</tr>
<tr>
<td>Focal segmental glomerulosclerosis</td>
<td>17</td>
<td>1.15</td>
</tr>
<tr>
<td>Lupus nephritis</td>
<td>11</td>
<td>0.74</td>
</tr>
<tr>
<td>Minimal change nephrotic syndrome</td>
<td>11</td>
<td>0.74</td>
</tr>
<tr>
<td>Alport syndrome</td>
<td>7</td>
<td>0.47</td>
</tr>
<tr>
<td>Normal</td>
<td>191</td>
<td>12.92</td>
</tr>
<tr>
<td>Other</td>
<td>36</td>
<td>2.44</td>
</tr>
<tr>
<td>Total</td>
<td>1478</td>
<td>100</td>
</tr>
</tbody>
</table>
A nationwide study of mass urine screening tests on Korean school children and implications for chronic kidney disease management

Byoung-Soo Cho · Won-Ho Hahn · Hae il Cheong · Inseok Lim · Cheol Woo Ko · Su-Young Kim · Dae-Yeol Lee · Tae-Sun Ha · Jin-Soon Suh

Published online: 08 November 2012

Conclusion Mass urine screening tests could detect asymptomatic GN in its early stages. Initial aggressive diagnosis and treatment for CHP and nephrotic-range groups may prove helpful as interventions that delay chronic kidney disease progression. These findings may
Adults

Screening for chronic kidney disease shows promise
The prognosis for patients who present late with chronic kidney disease can be poor in low-income countries. Could screening for the condition help change this situation? Tony Kirby reports.

Children

A Cost-effectiveness Analysis of Screening Urine Dipsticks in Well-Child Care

CONCLUSIONS: Urine dipstick is inexpensive, but it is a poor screening test for CKD and a cost-ineffective procedure for the primary care provider.

But ...
Children at risk

- Family history of chronic kidney disease
- Prematurity and/or Low birth weight
- Solitary kidney or major nephro-urologic malformations
- Obesity
- Hypertension
- Previous History of Acute Kidney Injury
- Growth retardation and polyuria
Urinalysis

Urinalysis is the physical, microscopic, and chemical examination of urine. It involves a number of tests to detect and measure various compounds that pass through the urine.

• Macroscopic appearance
  Visual examination of the urine sample for color and clearness.
Normal urine is clear and light yellow in color
Red urine
Case presentation: MR

A 4-year-old boy, with an uneventful previous history, passed reddish urine following 2 days of high fever, treated with amoxiclav and aminophenazone because of a positive strep test. Of the following choices, your first step would be:

1. Obtain a urinary tract US

2. Obtain blood chemistry for renal function and Complement evaluation

3. Obtain a dipstick and a microscopy evaluation of urine

4. Both answers 1 and 2
Case presentation: MR

A 4-year-old boy, with an uneventful previous history, passed reddish urine following 2 days of high fever, treated with amoxiclav and aminophenazone because of a positive strep test. Of the following choices, your first step would be:

1. Obtain a urinary tract US
2. Obtain blood chemistry for renal function and Complement evaluation
3. Obtain a dipstick and a microscopy evaluation of urine
4. Both answers 1 and 2
Case presentation: MR

Dipstick shows absence of hemoglobin and traces of proteinuria, while the microscopic urine evaluation shows the presence of hyaline casts. **Which one** of the following diagnoses would you consider?

1. Acute glomerulonephritis

2. Urinary tract infection

3. Pseudo hematuria due to NSAIDs

4. None of the previous answers
Case presentation: MR

Dipstick shows absence of hemoglobin and traces of proteinuria, while the microscopic urine evaluation shows the presence of hyaline casts. Which one of the following diagnoses would you consider?

1. Acute glomerulonephritis
2. Urinary tract infection
3. Pseudo hematuria due to NSAIDs
4. None of the previous answers
## Reddish urine dd

<table>
<thead>
<tr>
<th></th>
<th>Gross Hematuria</th>
<th>Hb-u</th>
<th>Mgb-u</th>
<th>Pigm-u</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Macroscopic appearance</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Dipstick</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td><strong>Microscopy</strong></td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Reddish urine

Dd: Hemoglobinuria
Myoglobinuria
Pseudohematuria or pigmenturia

✓ of endogenous origin (urates, bile pigments, porphyrin, homogentisic acid)

✓ of exogenous origin (beetroot, rhubarb, blackberries, blueberries, food colourings, rifampicin, para-aminosalicylates, nitrofurantoin, desferioxamine, vitamin B12, iodates)
10-year-old boy, with a previous uneventful history. Two hours after a football match painful micturition with bright red urine and some small clots. A unilateral costolumbar pain is also present. A microscopic urine evaluation shows isomorphic erythrocytes. Your suspicion is that this is a urologic hematuria because of:

1. Bright red color of the urine

2. Presence of small clots

3. Presence of isomorphic erythrocytes

4. All of the previous
Case presentation: GF

10-year-old boy, with a previous uneventful history. Two hours after a football match painful micturition with bright red urine and some small clots. A unilateral costolumbar pain is also present. A microscopic urine evaluation shows isomorphic erythrocytes. Your suspicion is that this is a urologic hematuria because of:

1. Bright red color of the urine
2. Presence of small clots
3. Presence of isomorphic erythrocytes
4. All of the previous
Case presentation: GF

For this boy, which of the following choices would be your first step:

1. Obtain a urinary tract US

2. Obtain blood chemistry for evaluation of renal function

3. Prescribe antibiotic treatment

4. Both answers 1 and 3
Case presentation: GF

For this boy, which of the following choices would be your first step:

1. Obtain a urinary tract US

2. Obtain blood chemistry for evaluation of renal function

3. Prescribe antibiotic treatment

4. Both answers 1 and 3
Macrophematuria

✓ Visible to the naked eye

✓ Urine colour varies from bright red to chocolate (depending on the pH, specific gravity and protein concentration)

✓ just 0.5 cc of blood in 100 cc of urine give the characteristic coloration
Macrohematuria - Incidence

- All patients with gross hematuria were reviewed at a pediatric emergency walk-in clinic over 24 consecutive months. Of a total of 128,395 patient visits, gross hematuria was proven in 158 (1.3/1,000 visits).

- Fifty-six percent of all patients had readily apparent causes for their gross hematuria. Twenty-six percent of all hematuric patients had documented urinary tract infections, but only 9% had apparent glomerular disease.

Ingelfinger JR et al - Pediatrics 1977
Macrohematuria

ASYMPTOMATIC OR ISOLATED

- no subjective symptoms
- origin and/or etiology of hematuria cannot be gleaned from medical history and physical exam

SYMPTOMATIC

- Positive medical history
- Edema, ↑BP, oliguria, ARF
- Skin eruptions
- Colic – articular pain
- Burning or urinary disorders
- Abdominal masses
Symptomatic Macrohaematuria: which tests for which diagnosis

- Symptoms of UTI → urinalysis and urine culture (virus)
- Trauma → ultrasound – CT scan
- Abdominal pain → ultrasound - screening for stones
- Nephritic Syndrome → proteinuria, kidney function, complement, autoantibodies.
- CKD in the family → + audiogram
- Ethnic background → haemoglobin panel (drepanocytosis)
  bladder schistosomiasis is the most common cause of hematuria in endemic areas, TBC
Between May 1979 and May 2002, 228 children were referred to the Authors center for evaluation of **asymptomatic gross hematuria**.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Gross Hematuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>228</td>
</tr>
<tr>
<td>Sex, M:F</td>
<td>161:67</td>
</tr>
<tr>
<td>White</td>
<td>210</td>
</tr>
<tr>
<td>African American</td>
<td>16</td>
</tr>
<tr>
<td>Asian American</td>
<td>2</td>
</tr>
<tr>
<td>Mean age at onset of hematuria, mo</td>
<td>104</td>
</tr>
<tr>
<td>Range</td>
<td>1-229</td>
</tr>
<tr>
<td>Mean age at first clinic visit, mo</td>
<td>111</td>
</tr>
<tr>
<td>Range</td>
<td>3-230</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Gross Hematuria (n = 228)</td>
</tr>
<tr>
<td>--------------------------------------------------------------------------</td>
<td>----------------------------</td>
</tr>
<tr>
<td>No diagnosis</td>
<td>86</td>
</tr>
<tr>
<td>Hypercalciuria without nephrolithiasian</td>
<td>51</td>
</tr>
<tr>
<td>Hypercalciuria with nephrolithiasian</td>
<td>2</td>
</tr>
<tr>
<td>IgA nephropathy</td>
<td>34</td>
</tr>
<tr>
<td>Post–streptococcal nephritis</td>
<td>21</td>
</tr>
<tr>
<td>Exercise</td>
<td>5</td>
</tr>
<tr>
<td>Thin basement-membrane disease*</td>
<td></td>
</tr>
<tr>
<td>Alport syndrome</td>
<td></td>
</tr>
<tr>
<td>Sickle cell trait</td>
<td></td>
</tr>
<tr>
<td>Mesangial proliferative nephritis</td>
<td></td>
</tr>
<tr>
<td><strong>Autosomal dominant polycystic kidney disease</strong></td>
<td></td>
</tr>
<tr>
<td>Membranoproliferative nephritis</td>
<td></td>
</tr>
<tr>
<td>Ureteropelvic junction obstruction</td>
<td></td>
</tr>
<tr>
<td>IgA nephropathy and hypercalciuria</td>
<td></td>
</tr>
<tr>
<td>Bilateral dysplasia</td>
<td></td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td></td>
</tr>
<tr>
<td>Solitary kidney</td>
<td></td>
</tr>
<tr>
<td>Wilms tumor</td>
<td></td>
</tr>
</tbody>
</table>

28% Glomerular causes

9% Other Urological causes

Asymptomatic Macrohematuria

“As clinically important abnormalities of the urinary tract are commonly discovered in children with asymptomatic gross hematuria, a thorough diagnostic evaluation is warranted”

Asymptomatic Macrohematuria
Algorithm

History + physical examination + urinalysis + US + RBC morphology

GLOMERULAR
- Proteinuria
- Kidney function
- C3, C4, IgA, TAS, anti nuclear Ab
- Urinalysis in parents and siblings
- Audiogram

NON GLOMERULAR
- Screening for stones
- Urine culture
- Kidney function
Evaluation of hematuria in children

Kevin E.C. Meyers, MBBCh

Causes of hematuria in children

**Glomerular diseases**
- Recurrent gross hematuria (IgA nephropathy, benign familial hematuria, Alport’s syndrome)
- Acute poststreptococcal glomerulonephritis
- Membranoproliferative glomerulonephritis
- Systemic lupus erythematosus
- Membranous nephropathy
- Rapidly progressive glomerulonephritis
- Henoch-Schönlein purpura
- Goodpasture’s disease

**Interstitial and tubular**
- Acute pyelonephritis
- Acute interstitial nephritis
- Tuberculosis
- Hematologic (sickle cell disease, coagulopathies von Willebrand’s disease, renal vein thrombosis, thrombocytopenia)

**Urinary tract**
- Bacterial or viral (adenovirus) infection-related
- Nephrolithiasis and hypercalciuria
- Structural anomalies, congenital anomalies, polycystic kidney disease
- Trauma
- Tumors
- Exercise
- Medications (aminoglycosides, amitryptiline, anticonvulsants, aspirin, chlorpromazine, coumadin, cyclophosphamide, diuretics, penicillin, thorazine)
Gross hematuria

Referral to a Pediatric nephrologist or urologist for

- **kidney biopsy** when:
  - proteinuria > 20 mg/Kg/die
  - prolonged RF (1 month)
  - presence of signs of systemic diseases
  - recurrence of macroematuria with persistence of glomerular microhematuria

- **cystoscopy**
Macrohematuria “To take home”

- Does not cause anemia
- If asymptomatic, it does not represent an emergency, but it needs attention
- Level of urgency dictated by associated symptoms
- Follow-up necessary (BP, urinalysis)
- If recurrent, see a specialist
Urinalysis

Urinalysis is the physical, microscopic, and chemical examination of urine. It involves a number of tests to detect and measure various compounds that pass through the urine.

• Macroscopic appearance

• Microscopic appearance
  – Dipstick
  – Light microscopy of urine samples
  – Microbiological culture

• Urine Chemistry
Specimen Collection

- Utilize the urine from the second urination of the morning

- **Clean-catch midstream urine collection** after thorough cleaning of the external genitalia is the most effective method.

- Urine should be collected in clean containers, ideally they should be sterile, even for non bacteriological tests.

- It is best to examine the urine **within 30 minutes** of collection; otherwise samples can be stored at +4 °C for no longer than 2 hours.
Work-up of abnormal urinalysis in primary care

• Microhematuria

• Proteinuria
**Case presentation: MV**

MV is an 8-year-old boy, whose family history reveals kidney stones in the maternal grandfather and a 48-year-old father who underwent surgery for PUJ obstruction. Past medical history: chickenpox and frequent tonsillitis between the ages of 4 and 8 years. At a routine sports medical check-up, physical examination and blood pressure were normal, growth at the 75th percentile, while urine dipsticks showed Hb++. What action should be taken?

1. Obtain a urinary tract US
2. Obtain a urinary tract US and blood chemistry for renal function
3. Repeat dipstick
4. No action
Case presentation: MV

MV is an 8-year-old boy, whose family history reveals kidney stones in the maternal grandfather and a 48-year-old father who underwent surgery for PUJ obstruction. Past medical history: chickenpox and frequent tonsillitis between the ages of 4 and 8 years. At a routine sports medical check-up, physical examination and blood pressure were normal, growth at the 75th percentile, while urine dipsticks showed Hb++. What action should be taken?

1. Obtain a urinary tract US
2. Obtain a urinary tract US and blood chemistry for renal function
3. Repeat dipstick
4. No action
ISOLATED HAEMATURIA

A frequent symptom in paediatric age:

1. Not to be overlooked as it can be an important indicator of kidney disease, even in the absence of proteinuria;

2. Not to be overestimated (especially persistent microscopic glomerular hematuria), with excessive medicalization of the child.

3. There are no indications for screening for hematuria in school-aged children.

4. Very few RBC are excreted into urine normally; normal excretion can be greater after exercise.
The Galveston study

Prospective study involving 12,252 children (6-12 years) which foresaw an annual urinalysis evaluation for 5 years.

- 4% of children had hematuria in the first urinalysis only
- 1% of children had hematuria in 2/3 consecutive urinalyses
- 0.5% of children had hematuria in 3/3 urinalyses on different days

Only 37% of the children with hematuria in at least 2/3 urinalyses had persistent hematuria after one year.
Asymptomatic Microhematuria

Urine Dipstick = + → ++++ (urine dipsticks are very sensitive. They show 0.02 - 0.03 mg/dl of HB or myoglobin = 5 -20 GR /ul)

- **transitory**: persists for less than 3-6 months
- **intermittent**: persists for more than 3-6 months, but is found in less than 50% of the tests performed
- **persistent**: persists for more than 3-6 months, but the tests are almost always positive (80→100%)
Localization of hematuria

- History
- Symptoms
- Urine analysis: proteinuria and RBC casts

<table>
<thead>
<tr>
<th>Distinguishing features of glomerular and nonglomerular hematuria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Feature</strong></td>
</tr>
<tr>
<td>History</td>
</tr>
<tr>
<td>Burning on micturition</td>
</tr>
<tr>
<td>Systemic complaints</td>
</tr>
<tr>
<td>Family history</td>
</tr>
<tr>
<td>Physical examination</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Edema</td>
</tr>
<tr>
<td>Abdominal mass</td>
</tr>
<tr>
<td>Rash, arthritis</td>
</tr>
<tr>
<td>Urine analysis</td>
</tr>
<tr>
<td>Color</td>
</tr>
<tr>
<td>Proteinuria</td>
</tr>
<tr>
<td>Dysmorphic red blood cells</td>
</tr>
<tr>
<td>Red blood cell casts</td>
</tr>
<tr>
<td>Crystals</td>
</tr>
</tbody>
</table>
Hematuria: A simple method for identifying glomerular bleeding
K.F. Fairley and D.F. Birch

Kidney Int 1982
Hematuria: a simple method for identifying glomerular bleeding.

Fairley KF, Kidney Int 1982
Dysmorphic red cells  Scanning microscopy showing dysmorphic red cells in a patient with glomerular bleeding. Acanthocytes can be recognized as ring forms with vesicle-shaped protrusions (arrows). Courtesy of Hans Köhler, MD
Mechanism of erythrocyte deformation: Red cells traverse through glomerular basement membrane

EXAMPLE OF PHASE-CONTRAST MICROSCOPY TEST *(glomerlar)*
EXAMPLE OF PHASE-CONTRAST MICROSCOPY TEST (*non-glomerlar*)
Criteria reported in the literature to classify a haematuria as glomerular or as probably glomerular

a) The presence of >80% dysmorphic erythrocytes
   Fasset, Lancet 1982
   De Santo, Nephron 1987
   Rath, Arch Dis Child 1990

b) the presence of ≥40% dysmorphic erythrocytes
   Van De Snoek, Lancet 1997
   Huussen Int J Clin Pract 2006

c) the presence of ≥5% acanthocytes/G1 cells
   Kohler, Kid Int 1991
   Kitamoto Nephron 1993
   Lettgen Pediatr Nephr 1995

d) the presence of erythrocytic casts
   Fogazzi, Oxf Un Press 1999
   Cohen, NEJM 2003
Red Blood Cell Morphology

glomerular RBCs  non glomerulare RBCs

quantitative proteinuria
kidney function
C3, C4, IgA
urinalysis parents and siblings
audiogram (familial forms)

kidney ultrasound scan
urinalysis to look for pyuria
test for significative bacteriuria
screening for stones
Causes of Glomerular Hematuria

- Acute post-infectious glomerulonephritis
- IgA Nephropathy
- Alport Syndrome
- Thin basement membrane disease/Benign Familial Hematuria
- Membranoproliferative glomerulonephritis
Causes of non-glomerular Hematuria

- UTI
- Hypercalciuria
- Kidney stones
- Polycystic kidney disease
- Strenuous exercise (long-distance running)
- Interstitial nephritis
- Drugs (anticoagulants)
Between May 1979 and May 2002, 342 children were referred to the Authors center for evaluation of asymptomatic microscopic hematuria.

- **No diagnosis** 80%
- **Hypercalciuria** 16.5%
- **Other causes** 3.5%
Microhematuria “To take home”

- Does not cause anemia
- If asymptomatic it does not represent an urgent problem and few tests are necessary
- Associated symptoms are important in the algorithm
- Monitoring of BP and urine dipstick is suggested
- Spontaneous resolution of microscopic hematuria is common
Work-up of abnormal urinalysis in primary care

- Microhematuria
- Proteinuria
MC, a 2-year-old girl, was born at 39 weeks via spontaneous delivery. BW 3,170g. Normal prenatal ultrasound. No notable illnesses. During an episode of fever, urine test for suspected UTI. Urinalysis shows sg 1034, pH 6, protein 1 g/L, Hb trace. Good general health, no edema, good statural and ponderal growth (Weight 13.7, H 83cm), BP 102/47

1. How should this be interpreted?

2. What should be done?

3. What should be said to the family?
Case presentation: MC

Dipstick urinalysis was repeated 3 days after defervescence of the fever and then again after 1 month: **no proteinuria**

1. What other tests are necessary?

2. Is an ultrasound scan useful?

3. What follow-up should be done?
Case presentation: FG

Personal and family medical history uneventful. Admitted to hospital with febrile convulsions (12 months), diagnosis of tonsillitis, antibiotic therapy. Urinalysis: sg 1022, pH 6, protein ++, Hb ++. A letter is written to the family doctor advising them to check urine test results, which was not done.

At the age of 18 months she arrives at A&E Department with gastroenteritis. Urinalysis shows protein 5.0 g/l; blood chemistry Creatinine 7.5 mg/dL, acidosis EB -18.6

**Diagnosis**: End stage renal failure

**Histological diagnosis**: Diffuse mesangial sclerosis
Case presentation: PA


What should be done?
NORMAL PROTEIN LEVELS IN CHILDREN’S URINE

Protein in a 24-hour urine sample :

   Premature babies   < 200 mg/m²  
   0 - 2 months       < 150 mg/m²   
   2 months - 14 years < 100 mg/m²  

Proteinuria/Creatininuria (mg/mg) :

   6 months - 2 years  < 0.5  
   > 2 years           < 0.25
Proteinuria Prevalence

Proteinuria was found in 10.7% of urine samples taken from 8,954 school-age children, who each provided 4 urine samples for testing.

However, only 0.1% of the population studied had positive urine protein levels in all 4 urine tests.
Glomerular and tubular proteinuria

D’Amico, Kidney Int., 2003
Proteinuria as a predictor of disease progression in children with hypodysplastic nephropathy

**Method**
- Number of children: 225
- M/F: 185/40
- Follow-up (Yrs): 3.5±1.1

**uPr/uCr:**
- A: < 0.2
- B: 0.2 - 0.9
- C: > 0.9

**Decline of renal function**

<table>
<thead>
<tr>
<th>Gruppo</th>
<th>Delta Ccr (ml/min/1.73mq/ad)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.2±3.62</td>
</tr>
<tr>
<td>B</td>
<td>-0.6±3.67</td>
</tr>
<tr>
<td>C</td>
<td>-3.76±5.64</td>
</tr>
</tbody>
</table>

*p<0.0001*
Asymptomatic Proteinuria - Algorithm

Positive Dipstick

Repeat weekly on 2 occasions

- STOP

Spot protein creatinine ratio
Split lying/supine or upright position

Orthostatic proteinuria
(BP and urinalysis/year)

Distinction between
Albumin
Likely glomerular disease

Tubular
Likely tubular diseases
Causes of isolated proteinuria

Intermittent

Transient
- Fever
- Dehydration
- Stress
- Exercise

Orthostatic
- most common cause of proteinuria in adolescents (75%);
- rarely exceeds 1 gm/day;
- secondary to (?) changes in glomerular hemodynamics due to postural changes
**Table 1: Causes of persistent proteinuria.**

<table>
<thead>
<tr>
<th>Glomerular</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diabetes</strong></td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
</tr>
<tr>
<td><strong>Reflux nephropathy</strong></td>
</tr>
<tr>
<td><strong>Primary glomerulonephropathy conditions</strong></td>
</tr>
<tr>
<td>Minimal change nephrotic syndrome</td>
</tr>
<tr>
<td>Focal and segmental glomerulosclerosis</td>
</tr>
<tr>
<td>Membranous nephropathy</td>
</tr>
<tr>
<td>Membranoproliferative glomerulonephritis</td>
</tr>
<tr>
<td>Congenital nephrotic syndrome</td>
</tr>
<tr>
<td><strong>Secondary glomerulonephropathy conditions</strong></td>
</tr>
</tbody>
</table>
### Table 1: Causes of persistent proteinuria.

<table>
<thead>
<tr>
<th>Tubulointerstitial</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acquired</strong></td>
</tr>
<tr>
<td>Acute tubular necrosis</td>
</tr>
<tr>
<td>Toxins (gold, lead, copper, and mercury)</td>
</tr>
<tr>
<td>Pyelonephritis</td>
</tr>
<tr>
<td>Interstitial nephritis (penicillins and other antibiotics, NSAIDs, and penicillamine)</td>
</tr>
<tr>
<td><strong>Inherited</strong></td>
</tr>
<tr>
<td>Proximal renal tubular acidosis</td>
</tr>
<tr>
<td>Cystinosis</td>
</tr>
<tr>
<td>Galactosemia</td>
</tr>
<tr>
<td>Lowe syndrome</td>
</tr>
<tr>
<td>Dents disease</td>
</tr>
<tr>
<td>Wilson disease</td>
</tr>
<tr>
<td>Tyrosinemia</td>
</tr>
</tbody>
</table>

Gattineni J 2012 Int J Ped