UNDERSTANDING URINALYSIS

**Interpretation of Urine Analysis**
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**Urine Analysis**
- Appearance or color
- Specific gravity
- pH
- Leukocyte esterase
- Nitrites
- Urobilinogen
- Bilirubin
- Glucose
- Ketones
- Protein
- Blood
- Microscopic examination

**Proper Specimen Collection**
- Teach every patient how to collect proper specimen
- 1. Clean-catch midstream
- 2. In patients with indwelling urinary catheters, a recently produced urine sample should be obtained (directly from the catheter tubing)
- 3. Best examined when fresh. Chemical composition of urine changes with standing and formed elements degenerate with time
- 4. Refrigerated is best when infection is suspected
- 5. First voided morning urine is ideal when evaluating suspected glomerulonephritis

**Routine Urine Analysis**
- Appearance
- Chemical tests (dipstick)
  - pH
  - Protein
  - Glucose
  - Ketones
  - Blood
  - Urobilinogen
  - Bilirubin
  - Nitrites
  - Leukocyte esterase
  - Specific gravity

**Microscopic examination of spun urinary sediment**

**Urine Analysis with Microscopy**

**Dipstick Methodology**
- Paper tabs impregnated with chemical reagents
- Reagents are chromogenic
- Reagents are timed developed
- Some rxns are highly specific
- Other are sensitive to the presence of interfering substances or extremes of pH
- **Rapid, semiquantitative assessment of urinary characteristics**
UNDERSTANDING URINALYSIS

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Urine Color Change

<table>
<thead>
<tr>
<th>Color</th>
<th>Substances</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>Chyle, pus, phosphate crystals</td>
</tr>
<tr>
<td>Pink/Red/Brown</td>
<td>Erythrocytes, hemoglobin, myoglobin, porphyrins, beets, senna, cascara,</td>
</tr>
<tr>
<td></td>
<td>levodopa, methylidopa, deferoxamine, metronidazole, phenacetin,</td>
</tr>
<tr>
<td></td>
<td>arthaquiones, doxorubicin, phenothiazines</td>
</tr>
<tr>
<td>Yellow/Orange/Brown</td>
<td>Bilirubin, urbin, phenazopyridine, urinary</td>
</tr>
<tr>
<td></td>
<td>2ndies, senna, cascara, mecapacine, iron compounds, nitrofurantoin,</td>
</tr>
<tr>
<td></td>
<td>riflocks, rhubarb, sulfasalazine, riflavin, fureseina,</td>
</tr>
<tr>
<td></td>
<td>phenytoin, metronidazole</td>
</tr>
<tr>
<td>Brown/Black</td>
<td>Methemoglobin, homogentisic acid, melanin, levodopa, methylidopa</td>
</tr>
<tr>
<td>Blue or green/Green/Brown</td>
<td>Biliverdin, Pseudomonas infection, dyes</td>
</tr>
<tr>
<td></td>
<td>[methylene blue, indigo carmine], triamterine, Vitamin B complex,</td>
</tr>
<tr>
<td></td>
<td>methocarbamol, indican, phenol, chlorophyll, propofol, amitriptyline,</td>
</tr>
</tbody>
</table>

Urine Specific Gravity

- Increased Urine Specific Gravity:
  - Diarrhea that causes dehydration
  - Heart failure
  - Dehydration
  - Diarrhea/emasis
  - Renal artery stenosis
  - Glycosuria
  - Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
  - Hepatorenal syndrome

- Decreased Urine Specific Gravity:
  - Acute tubular necrosis
  - Interstitial nephritis
  - Diabetes insipidus
  - Drinking too much fluid
  - Kidney failure
  - Pyelonephritis

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Urine pH

- Physiologic urine pH ranges from 4.5 to 8
- Most accurate if done promptly
- Not sufficiently accurate to be used for diagnosis of renal tubular acidosis (check ABG and urine lytes)
- Changing urine pH to either acidic or alkaline may prevent development of certain types of kidney stones

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Leukocyte Esterase

- Detects esterase, an enzyme released by WBC
- Reflects presence of pyuria and may be used to detect > 10 leukocytes per HPF
- False negatives can occur in the presence of
  1. Glycosuria
  2. High specific gravity
  3. Cephalexin or tetracycline Tx
  4. Excessive oxalate excretion
- False positives can occur with contamination of vaginal debris and trichomonas infection

Nitrites

- Screening test for bacteriuria
- Reflects presence of >10(5)CFU of Enterobacteriaceae per ml of urine
- Relies on ability of **gram-negative bacteria** to convert nitrate → nitrite
- False negative can occur
  1. Bacteria that cannot convert nitrate → nitrite:
  - **EX:** Enterococcus
  2. Presence of ascorbate
  3. Retention of urine in bladder ≤4 hours
  4. Decrease in urine pH
- False positive can occur with substances that turn urine red such as use of bladder analgesic phenazopyridine or ingestion of beets

Ms. Smith is a 38yo who presents with 4 days of dysuria, frequency, urgency and foul smelling urine. UA reveals positive nitrite and leukocyte esterase. You empirically start her on Bactrim for treatment of presumed UTI.
UNDERSTANDING URINALYSIS

UTI

- Symptoms of dysuria, frequency, urgency, suprapubic pain and/or hematuria
- Uncomplicated: healthy non-pregnant adult women
- Dipstick urine analysis without urine culture is sufficient for Dx of uncomplicated UTI
- Sensitivity of 75% and specificity of 82% when positive for either leukocyte esterase or nitrite.

Bacteria, Yeast and other Infectious Agents:
- May discern between cocci and bacillary forms of bacteria on unstained urine sample
- Individual and budding yeast and hyphal forms occur with Candida
- Trichomonas are identified by their tear drop shape and motile flagellum

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Urobilinogen and Bilirubin

- Urobilinogen produced in the gut from metabolism of bilirubin. Excreted in feces and urine.
- In obstructive jaundice, bilirubin does not reach bowel, so urinary excretion of urobilinogen is diminished
- In other forms of jaundice, urinary urobilinogen is increased
- Better tests are available to diagnose obstructive jaundice

Glucose (glycosuria)

- Dipstick is specific for glucose.
- Rely on glucose oxidase to catalyze the formation of hydrogen peroxide
- High concentrations of ascorbic acid can result in false-negative test
- Due to inability of kidney to reabsorb glucose in PT despite normal serum glucose or urinary spillage with high serum glucose
- Normal renal function: glycosuria does not generally occur until serum glucose exceeds 180mg/dl

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Ketones

- Created when body breaks down fat or fatty acids for energy instead of carbohydrates or sugar
- Measures the presence of urine ketones
- False positive may occur with usage of levodopa, captopril (drugs containing free sulfhydryl group)
- Ordered when patient has Type 1 DM AND diabetic ketoacidosis is suspected particularly when patient is sick
- Monitored in a person...
  1. On a low-carbohydrate and/or high-fat diet
  2. Not able to eat (anorexia/fasting), is vomiting and/or diarrhea
  3. Pregnant woman who has DM or gestational DM

Proteinuria

<table>
<thead>
<tr>
<th>Level</th>
<th>mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trace</td>
<td>0-15</td>
</tr>
<tr>
<td>1+</td>
<td>15-30</td>
</tr>
<tr>
<td>2+</td>
<td>30-100</td>
</tr>
<tr>
<td>3+</td>
<td>100-300</td>
</tr>
<tr>
<td>4+</td>
<td>&gt;300</td>
</tr>
</tbody>
</table>

Mr. Jones is an 84yo male who presents with chronic and progressive generalized weakness, 20lbs weight loss and pain in back particularly induced with movement. Labs reveal: serum creatinine 2.5mg/dl, serum calcium 11.0mg/dl, hemoglobin 9.8g/dl. UA dipstick was negative for proteinuria or hematuria. 24 hour urine revealed 2.5grams of total protein.

Multiple Myeloma - neoplastic proliferation of immunoglobulin-producing plasma cells

- Initial screening SPEP, 24hr urine UPEP, and immunofixation
- DDX: MGUS, SMM, Waldenstrom macroglobulinemia, AL amyloidosis, solitary plasmacytoma, POEMS syndrome and metastatic carcinoma
**Urine Protein Composition**

<table>
<thead>
<tr>
<th>PLASMA PROTEINS</th>
<th>EXCRETION (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>12</td>
</tr>
<tr>
<td>Immunoglobulin G</td>
<td>3</td>
</tr>
<tr>
<td>Immunoglobulin A</td>
<td>1</td>
</tr>
<tr>
<td>Immunoglobulin M</td>
<td>0.3</td>
</tr>
<tr>
<td>Light Chains</td>
<td></td>
</tr>
<tr>
<td>kappa</td>
<td>2.3</td>
</tr>
<tr>
<td>gamma</td>
<td>1.4</td>
</tr>
<tr>
<td>Beta-Microglobins</td>
<td>0.12</td>
</tr>
<tr>
<td>Other plasma proteins</td>
<td>20</td>
</tr>
<tr>
<td>Nonplasma-Tamm-Horsfall protein</td>
<td>40</td>
</tr>
<tr>
<td>Other non-renal-derived proteins</td>
<td>&lt;1</td>
</tr>
<tr>
<td><strong>TOTAL PROTEINS</strong></td>
<td><strong>80</strong></td>
</tr>
</tbody>
</table>

**Proteinuria**
- Highly sensitive to albumin AND insensitive to other urinary proteins such as globulins, hemoglobin, or light chains
- Scored from trace to 4+ based on concentration
- Quantification is influenced by urine concentration: dilute urine may give falsely low results
- Ranges from 200-3000mg/24hour are readily detected
- Not sensitive enough to detect for MICROALBUMINURIA
- Highly alkaline urine may produce false-positive rxns
- IF proteinuria other than albumin is suspected, more sensitive assays should be used (SPEP, UPEP IFE, serum free light chains)

**Quantification of Proteinuria**
- If presence of proteinuria is detected on dipstick, confirmation is required through quantification of proteinuria.
- Measurement of urinary protein
  1. 24 hour total urinary protein
  2. Random protein/creatinine or albumin/creatinine. Adjustment for urinary protein concentration is made by relating the urine protein concentration to the urine creatinine concentration

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  - Microscopic examination

**Hematuria**

**Urinary RBC vs WBC**
Mr. Smith is a 27yo male who presented to the emergency room after 2 days of nausea, vomiting, myalgias and "kool aid" colored urine. He states that he is in the police academy in Dallas and he started intensive "boot camp" last week during the first week of August. UA was positive for blood but microscopy did not reveal urinary RBC.

**Hematuria**

- Dipstick relies on the peroxidase activity of hemoglobin to catalyze an organic peroxide with subsequent oxidation of an indicator dye
- Myoglobin is also detected because it has intrinsic peroxidase activity
- Suspect myoglobinuria or hemoglobinuria with positive by dipstick but negative for urinary RBC by microscopic examination
- Confirm all positive dipsticks with microscopic examination of spun urinary sediment vs supernatant

**False Positive Hematuria**

- Presence of semen in urine may cause positive heme reaction
- Alkaline urine with pH>9 or contamination with oxidizing agents used to clean perineum
- Presence of myoglobinuria

**Mimics of Hematuria**

- Menstrual cycle: remember age and sex of patient
- Ingestion of beets, rhubarb, certain food dyes or senna: what is your patient eating?
- Drugs: pyridium, phenytoin, rifampin, nitrofurantoin

**Hematuria**

- Is common, particularly young adult patients, hematuria is transient and of no consequence
- Can be transient or persistent (history is very important)
- Grossly visible (macroscopic) or detectable only on urine examination (microscopic)
- Pathology represents the presence of 3 or more RBC per high power field (HPF) in a spun urine sediment
- Dipstick for heme detect 1 to 2 RBC per HPF
- Dipsticks are at least as sensitive as urine sediment examination, but result in more false positive tests
- Positive dipstick test needs to be confirmed with microscopic evaluation

Where is the origin of the hematuria?
Causes of Hematuria

1. Renal: renal mass, glomerular pathologies, structural disease, pyelonephritis, malignant HTN, renal vein thrombosis, AV malformation, papillary necrosis (sickle cell)
2. Ureter: malignancy, stone, stricture, fibroepithelial polyp
3. Bladder: malignancy, radiation, cystitis
4. Prostate/urethra: BPH, malignancy, prostatic procedures, traumatic catheterizations, urethritis, urethral diverticulum

Distinguishing Extraglomerular from Glomerular Hematuria

<table>
<thead>
<tr>
<th></th>
<th>Extraglomerular</th>
<th>Glomerular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>Red or pink</td>
<td>Red, smoky brown or coca-cola (due to prolonged transit thru nephron and an acid urine pH may result in the formation of methemoglobin)</td>
</tr>
<tr>
<td>Clots</td>
<td>May be present</td>
<td>Absent</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>&lt;500mg/day</td>
<td>May be &gt;500mg/day</td>
</tr>
<tr>
<td>RBC morphology</td>
<td>Normal</td>
<td>Some RBC are dysmorphic with blebs, budding, segmental loss of membrane resulting in marked variability of RBC shape</td>
</tr>
<tr>
<td>RBC casts</td>
<td>Absent</td>
<td>May be present</td>
</tr>
</tbody>
</table>

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Microscopic Examination of the Spun Urine Sediment

1. Cellular elements
   - RBC
   - WBC
   - Renal tubular epithelial cells
   - Squamous cells of urethral, vaginal or cutaneous origin
   - Transitional epithelial cells line the renal pelvis, ureter, bladder and proximal urethra
2. Casts
Cellular Elements

Urinary Casts

• Named based upon shape and origin
• Consist of a matrix of Tamm-Horsfall urinary glycoprotein in the shape of the distal tubular or collecting segment where they were formed
• Matrix has a straight margin compared to clumps of cells or debris has seen in cellular elements
• Formation in pronounced during low flow, concentrated salts and low pH

Urinary Casts

Formed via precipitation of Tamm-Horsfall mucoprotein in the distal convoluted tubule and collecting ducts.

Hyaline Casts
Consists of protein alone. Difficult to see b/c of refractive index is close to that of urine.

Waxy/Broad Casts
Consists of hyaline material with a much greater refractive index.

RBC Cast
WBC Cast
Granular Cast
Consists of finely (altered serum protein) or coarsely (degeneration of embedded cells) granular material.

Tubular Cell Cast
Consists of sloughed epithelial tubular cells.

Hyaline Cast
Nonspecific, solidified Tamm-Horsfall mucoprotein. Most common cast. Ex: normal individuals in dehydration or vigorous exercise.

Waxy/Broad Casts
Form in tubules that have become dilated and atrophic due to chronic parenchymal disease.

Granular Cast
Characteristically seen with acute tubular necrosis (ATN) and toxic ingestion, such as mercury, diethylene glycol or salicylate. But can occur in concentrated urine.

Urinary Crystals
- Formation is dependent on degree of concentration of constituent molecules, urine pH, and the presence of inhibitors of crystallization
- May be present spontaneously or may precipitate with refrigeration of urine
Objectives: Urine Analysis

- To understand the basics of urine analysis both dipstick (UA) and microscopy (UA with micro) and how results related to clinical practice
- Appearance or color
- Specific gravity
- pH
- Leukocyte esterase
- Nitrites
- Urobilinogen
- Bilirubin
- Glucose
- Ketones
- Protein
- Blood
- Microscopic examination

Thank you for your time

Questions?

Disclosure Statement

- Research: Ardelyx
- Speakers Bureau: Amgen and Merck
- Consultant: Amgen, Merck, Boehringer-Ingelheim, Stealth Peptides, BMS, and Clegene

Understanding the Importance of Proteinuria

National Kidney Foundation Annual Meeting
Advanced Practitioner Program
Gaylord, Texas
April, 2015
Robert D. Toto, M.D., Professor of Medicine
Medical Director, Kidney Liver Pancreas Clinic
Director, Patient Oriented Research in Nephrology
UT Southwestern Medical Center

- Causes and Mechanisms
- Diagnosis and Detection
- Clinical Relevance
- Treatment
  - Primary cause
  - Dietary sodium restriction
  - RAAS blockade
  - Complications
Case: part A

• A 70 y/o white male presents with a 3 mo. History of peripheral edema.

• Does not smoke, drink or use drugs.

• No fever, rash, nocturia, weight loss, joint pain, hemoptysis or hematuria.

Case: part B

• Exam: BP 160/100, 1+ ejection murmur, ascites, 4+ pitting edema.

• Cr 1.4 mg/dl; Serum albumin 1.4 g/dl (nl 4-5 g/dl)

• FBG 109 mg/dl; LDL cholesterol 220 mg/dl

• 24-hour urine protein 8 g; Ccr 54 ml/min/1.73 m²

Diagnosis

Nephrotic Syndrome

I would now do the following

• Serum protein electrophoresis
• Urine protein electrophoresis
• Serologies
• Renal Biopsy
• All of the above
• None of the above

The most likely diagnosis is

• Focal segmental glomerulosclerosis
• Membranous nephropathy
• Diabetic nephropathy
• Multiple myeloma

Case: Diagnosis and Treatment

• Renal Biopsy: Membranous glomerulopathy

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New Insights into Membranous Nephropathy

Podocyte Proteins and Glomerular Disease

Antibody to Phospholipase A2 Receptor in Membranous Nephropathy

Antibody and Disease Activity in a Patient with Membranous Nephropathy

Case: Diagnosis and Treatment

- Renal Biopsy: Membranous glomerulopathy
- Rx: Cytoxan 100 mg/d x 1 month alternating with prednisone 1.0 mg/kg/d x 6 months
- 2 gram sodium diet
- Lisinopril 40 mg once daily

Many diseases can Cause Nephrotic Syndrome

- **Primary glomerular diseases**
  - Membranous nephropathy
  - Focal sclerosis
  - Membranoproliferative GN
  - IgA nephropathy
  - IgM nephropathy
  - Fibrillary GN
  - Immunotactoid nephropathy
  - C1q nephropathy
  - Post-infectious GN, etc.

- **Secondary glomerular diseases**
  - Diabetes
  - SLE
  - Amyloidosis
  - Cancer lymphoma, solid tumors
  - Hepatitis B and C
  - Drugs
    - NSAIDS, Gold, pamidronate
    - Other

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Types of Proteinuria

<table>
<thead>
<tr>
<th>Type</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glomerular</td>
<td>Glomerulonephritis</td>
</tr>
<tr>
<td>Tubular</td>
<td>Tubulointerstitial nephritis (e.g., due to drug)</td>
</tr>
<tr>
<td>Overflow</td>
<td>Myeloma</td>
</tr>
</tbody>
</table>

What is the Basis of Glomerular Proteinuria?

Normal: Glomerular Permeability to Albumin is Restricted
ENDOTHelial Injury: Glomerular Permeability to Albumin Increased

- Bowman’s Space
- Slit Diaphragm
- Damaged Endothelium
- Albumin Leak
- Increased hydrostatic pressure

**Diagnosis and Detection of Proteinuria**

**Proteinuria and Microalbuminuria**

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Proteinuria</th>
<th>Microalbuminuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine dipstick</td>
<td>Total protein</td>
<td>Albumin only</td>
</tr>
<tr>
<td>Method of estimate*</td>
<td>Protein / Creatinine ratio</td>
<td>Albumin / Creatinine ratio</td>
</tr>
<tr>
<td>Abnormal level</td>
<td>&gt; 0.15 g Prot / g Cr</td>
<td>&gt; 30 mg / g creatinine</td>
</tr>
<tr>
<td>Renal Significance</td>
<td>Glomerular: accelerated decline in renal function</td>
<td>Marker incipient diabetic nephropathy</td>
</tr>
<tr>
<td></td>
<td>Tubular: sign of TIN</td>
<td></td>
</tr>
<tr>
<td>Increased CV Risk</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* Spot urine preferably A.M. sample

**Common Causes of Albuminuria**

- Diabetes Mellitus
- Hypertension
- Atherosclerotic vascular disease
- Smoking

**Detecting Proteinuria in Routine Urine Analysis**

- If persistently > trace positive (≥ 2 occasions) deserves further evaluation
- Glomerular or tubular disease or both
- Detection limit is about 300 mg/L
- Misses
  - Microalbuminuria, e.g. diabetes
  - Light chain nephropathies
- Urine albumin/creatinine ratio
Quiz

- 70 year old man with type 2 DM c/o fatigue and found to have Scr 1.7 mg/dl
- Exam: BP 130/70, unremarkable
- Urinalysis negative for protein negative, no cells, casts, crystals
- 24 hour urine Ccr 42 ml/min
- 24 hour urine protein 4,200 mg

The most likely diagnosis is

- Focal segmental glomerulosclerosis
- Membraneous nephropathy
- Diabetic nephropathy
- Multiple myeloma

PEAKL: Dipstick does not detect light chains

Evaluation of Proteinuria

- Proteinuria detected by dipstick
- Confirm by random Uprot/Ucr ratio
- Or 24 hour urine
- Serologies
- SPEP and UPEP
- Immunofixation
- Biopsy

Method for Detecting Microalbuminuria

- First morning urine void (preferred)
- Urine albumin concentration
- Urine creatinine concentration
- Calculate albumin/creatinine ratio

Clinically meaningful use of albuminuria

- Screening Test
- Monitoring Disease activity
  - Normal kidney
  - Eclampsia kidney

Prognostic Significance of albuminuria

- Albuminuria and progression of kidney disease
- Albuminuria and cardiovascular disease
- Albuminuria and mortality

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Who Should Be Treated?

- Patients with microalbuminuria (30-299 mg/g)
  - Diabetes
  - Hypertension
  - Biopsy proven kidney disease
- Kidney disease with macroalbuminuria ≥ 300 mg/g

Treatment

Rationale for Lowering Albuminuria

- Increases risk for cardiovascular events
- Accelerated decline in kidney function

How to Treat

- Underlying Cause whenever possible, e.g. immunosuppression for lupus
- Dietary sodium restriction
  - Enhances antiproteinuric effect of ACEi/ARB
  - Helps lower BP in hypertensive patients
- Pharmacologic lowering of blood pressure in hypertensives
  - RAAS Blockade
  - Additional antihypertensives including diuretics
- Avoid NSAIDS (salt retention)

How Much Does a RAAS Blocker Lower Proteinuria?

- Overall about 50%
- Variable, depending on effect on
  - Systemic Blood pressure
  - Efferent Arteriole resistance
  - Glomerular Basement Membrane

How Much Does a RAAS Blocker Lower Proteinuria?
Effect of Salt Intake on Proteinuria in ACEi Treated Patient

- Baseline
- ACEi + Lo Salt
- ACEi + Hi Salt

Management of Albuminuria

- Lower BP to < 130/80 mmHg
- Use a once-daily ACEi or ARB
- Titrate ACE inhibitor to maximal recommended dose
- Lower urine alb/cr ratio to < 300 mg/g

ACE inhibitors and Angiotensin Receptor Blockers Slow Progression of Kidney Disease in Hypertensive Type 2 Diabetics

Albuminuria (µg/min)

- Overt nephropathy
- Microalbuminuria
- Normoalbuminuria

Clinical Trials

- IDNT
- RENAAL
- IRMA 2
- BENEDICT

What about Combination Rx

Combination Rx with Drugs that Block RAAS

- Greater reduction in proteinuria
- Small or no further reduction in BP
- No improvement in long-term outcome (ESRD and CV events)
- Higher incidence of complications

The Renin Angiotensin System: Strategies for Blockade

- Angiotensinogen → Renin → Ang I → Ang II
- ACEi/DRI/ARB
- AT1 receptor
- Aldosterone
- Adrenal Zona Glomerulosa

Combination Rx with Drugs that Block RAAS

- Greater reduction in proteinuria
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**Understanding Urinalysis**

**Slides**

**Randomized Double-Blind Placebo-Controlled Trial**

<table>
<thead>
<tr>
<th>Run-in</th>
<th>Double-Blind</th>
<th>W/O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lisinopril 80 mg daily and SBP goal &lt;130 mm Hg</td>
<td>Placebo daily</td>
<td></td>
</tr>
<tr>
<td>N = 81 Type 1 and 2 diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two 24-hour UACR ≥ 300 mg/g</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Inpatient CTRC: 24 hour ABP, creatinine clearance and urine albumin/creatinine ratio

**Suppression of urinary albumin excretion by combined use of Losartan or Spironolactone**

**Serum Potassium Concentration**

- **Spirinolactone**
- **Placebo**
- **Losartan**

**Perils of Higher Dose ACEi/ARB in Treatment of Proteinuria**

- **Proteinuria**
- **AKI**
- **K**
- **BP**

**Combining ACEi and ARB: Large Scale Clinical Trials**

- **1ALTITUDE Study**: Combined ACEi or ARB with a Direct Renin Inhibitor in Type 2 diabetes: No benefit, more hyperkalemia
- **2NEPHRON-D Study**: Combined ACEi and ARB in type 2 diabetes: Stopped for futility, more hyperkalemia
- **3ONTARGET Study**: Combined ACEi and ARB: No benefit, more acute kidney injury, hyperkalemia, hypotension

**Indications for Nephrology Referral**

- Hematuria/proteinuria unexplained
- Estimated GFR < 80 ml/min
- Nephrotic Syndrome
- Uncontrolled hypertension
- Need for Renal Biopsy
  - SLE, Necrotizing vasculitis, other
UNDERSTANDING URINALYSIS

Slides

THE END