The Kidney/Urinary Tract—

Structure-Function Correlation

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Basic Mechanisms of Disease
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Renal Pelvis, Ureters, Bladder, Urethra

- Conduit for urine = glomerular filtrate of blood as modified by tubules in the kidney
- Ureters – move urine by peristalsis
- Bladder – muscular reservoir for urine – openings for ureters (in) and urethra (out) - controlled by sphincters
- Urethra – short (females) or long (males) - neurological control of sphincter
The Urinary Tract

- What can go wrong?
- Obstruction – silent or painful- tumors, strictures, stones
- Infection- fever/pain- bacterial, fungal
- Congenital abnormalities- hypospadias, valves and strictures, deformities
- Neoplasms – some associated with toxins – cigarettes, aniline dyes (includes prostate)
- Trauma, including instrumentation
Unilateral Obstruction

Pelvi-ureteric junction obstruction
Calculus, tumour, blood clot or sloughed papilla in ureter
Stricture: tumour, tuberculosis
Extrinsic invasion from cervical, rectal or sigmoid carcinoma
Bladder tumour
Prostatic enlargement
Urethral valves
Urethral stricture

Intravenous pyelogram w/ contrast
Hydronephrosis of the Kidney
POLAR SCARS - VESICOURETERAL REFLUX
The Kidney - Functions

- Regulation of blood volume
- Regulation of body water, solutes (Na, K, Cl, S, P, Ca), osmolality (with GI tract)
- Control of pH of body fluids (with lung)
- Filtration of toxins (with liver)
- Metabolic – gluconeogenesis
- Endocrine – eg BP control (renin-angiotensin), hematopoiesis (erythropoietin)
### TABLE 1: SOME NORMAL HUMAN VALUES

(From FASEB Biological Data Reference Book; Values in parenthesis limit the 95% range)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unit</th>
<th>Value</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺</td>
<td>meq/liter</td>
<td>138</td>
<td>(132 - 144)</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>meq/liter</td>
<td>102</td>
<td>(97 - 108)</td>
</tr>
<tr>
<td>pH</td>
<td>Arterial</td>
<td>7.39</td>
<td>(7.34 - 7.44)</td>
</tr>
<tr>
<td></td>
<td>Venous</td>
<td>7.35</td>
<td>(7.28 - 7.42)</td>
</tr>
<tr>
<td>CO₂ Content (mM)</td>
<td>Arterial</td>
<td>26.9</td>
<td>(25 - 29)</td>
</tr>
<tr>
<td></td>
<td>Venous</td>
<td>29.6</td>
<td>(26 - 33)</td>
</tr>
<tr>
<td>PCO₂ (mm Hg)</td>
<td>Arterial</td>
<td>41.6</td>
<td>(35 - 47)</td>
</tr>
<tr>
<td></td>
<td>Venous</td>
<td>50</td>
<td>variable</td>
</tr>
<tr>
<td>Plasma volume</td>
<td>% body weight</td>
<td>4.5</td>
<td>(3.9 - 6.2)</td>
</tr>
<tr>
<td>Blood volume</td>
<td>% body weight</td>
<td>7.8</td>
<td>(6.4 - 9.7)</td>
</tr>
</tbody>
</table>
The Glomerulus - I

- Primary site of plasma filtration – fluid from blood to proximal tubule
- Capillary tuft supplied by afferent arteriole - high pressure
- Blood exits via efferent arteriole - arterioles can differentially dilate, constrict to control capillary pressure, filtration
The Glomerulus - 2

- Capillary wall formed by endothelium, basement membrane, and epithelium ("podocytes")
- Physical "pores" in filter - size restrictive (< 5200 d, < 14A radius filtered; > 34000 d not filtered)
- Surface charge – anionic - charge restriction
- Filtration pressure is balance of blood pressure in capillaries, osmotic pressure of plasma proteins that are not filtered
- Filtrate – water, electrolytes, sugars, amino acids, drugs, toxins
The Glomerulus- 3

- Mesangium – support structure for capillaries
- Mesangial cells
  - are phagocytic
  - can contract
  - produce matrix
  - produce/react to cytokines, hormones
Normal Glomerulus - Histology
Normal Glomerulus

- Epithelial cell
- Foot processes
- Basement membrane
- Endothelial cell
- Capillary lumen
- Mesangial cell
- Mesangial matrix
The Podocyte

A post-mitotic cell with highly specialized structure and function specific to the glomerulus.

- Regulate permselectivity
- Structural support for capillary
- Remodeling GBM
- Endocytosis of filtered proteins
- Counteract hydrostatic pressure
Molecular Anatomy of the Podocyte
EM - Glomerular filter
Hydraulic Pressure profile

- Renal Artery
- Afferent arteriole
- Glomerular Capillaries
- Efferent arteriole
- Peritubular Capillaries
- Intratubular veins
- Renal Vein

Pressure in mm Hg.
Glomerular Filtration Rate

- Clearance of molecule used as a tracer - must be freely filtered at glomerulus, not metabolized, not absorbed or secreted by tubules, non-toxic
- $U[\text{tracer}] \times \text{Volume of Urine} / P[\text{tracer}]$
- Normal for adults – 80-120 cc/min, lower for children
- Internal marker – creatinine (a protein released at a constant rate from muscle)
- External marker – inulin (a sugar)
The glomerulus

What can go wrong?
- Proteinuria
- Hematuria
- Loss of filtration

Causes of injury/disease
- Trauma/physical insults (eg radiation)
- Ischemia
- Infection – direct or indirect (inflammation)
- Immune diseases (inflammation)- lupus; post-infectious
- Toxins - including drugs (eg NSAIDs)
- Metabolism/endocrine- diabetes
- Congenital/genetic- podocyte defects
Normal Glomerulus

- Epithelial cell
- Foot processes
- Basement membrane
- Endothelial cell
- Capillary lumen
- Mesangial cell
- Mesangial matrix
Proteinuria is Associated with Foot Process Effacement

Figure 20-18. A. Ultrastructural characteristics of minimal change disease: loss of foot processes (double arrows), absence of deposits, vacuoles (V) and microvilli in visceral epithelial cells (single arrow). B. Schematic representation of minimal change disease, showing diffuse loss of foot processes.
Minimal Change Disease
FSGS - Collapsing Variant, with podocyte hyperplasia
Diabetic Glomerulopathy with Arteriolar Hyalinosis
Membranous Glomerulopathy
Hematuria often associates with increased glomerular cellularity
Post-infectious GN

- Immune complexes
- Proliferated endothelial cells
- Increased mesangial cells
- BM
Immune complexes
Red cell casts in the urine
Kidney Tubules - Function

- Reabsorb filtered electrolytes, nutrients, water – would dessicate or need to drink constantly without this
- Secrete substances – endogenous and exogenous (drugs, toxins)
- Regulate pH – via HCO3, ammonium ion
- Produce relatively concentrated or dilute urine depending on fluid volume, osmolality
Nephron Segments - Proximal

- High rate of reabsorption of NaCl and water: pumps, porters, channels
- Absorbs all of the glucose, amino acids, HCO3 from filtrate (Na-coupled) plus small proteins
- Cells have elaborate apical brush border and BL infoldings, mitochondria
- Reabsorption driven by Na:K ATPase at BL surface: requires energy
- 180L filtered/day: reabsorbs 120 L
NORMAL TUBULOINTERSTITIUM - PAS STAIN
NORMAL POLARIZED TUBULAR EPITHELIUM
“Loop of Henle” - creates highly concentrated milieu in renal medulla – NaCl, urea

Early portion – absorbs water (many channels)

Mid-late portion – absorbs NaCl, impermeable to water

Na:K ATPase drives transport

60L/day arrive from proximal tubule- absorbs 35L
Nephron Segments - Distal

- Absorbs NaCl, water
- Absorption regulated by hormones as tubular segments traverse the medulla - controls numbers of water channels in cell membranes
- Receives 25 L, reabsorbs 23-24 L
- Final urine – 1-2 L/day
SOLUTE COUPLED WATER MOVEMENT:

- Solute Coupled water transport
- Water channels
- Apical cell membrane
- Basolateral cell membrane
Anti-Diuretic Hormone

- Released from pituitary in response to increase in/high extracellular fluid osmolality
- Regulates water permeability of collecting ducts, urea cycling in interstitium
- If ADH low- tubular fluid will be less concentrated in loop of Henle, dilute in collecting duct (water trapped in fluid)- urine dilute
- If ADH high – tubular fluid very concentrated in loop of Henle, very concentrated in collecting duct (water moves out in response to “salty” milieu)
SUMMARY OF WATER
Response to an Increase in ECF Osmolality

Osmolality ↑

↑ ADH → ↓ Renal water output → Net water gain ↑ → Restore normal osmolality

Thirst ↑ → ↑ Water intake
Response to a Decrease in ECF Osmolality

Osmolality↓

↓ ADH

↑ Renal water output

↓ Thirst

↓ Water intake

↑ Net water loss

Restore normal osmolality
Control of body fluid volume, Na

Sensors
- Baroreceptors- aortic arch, carotid sinus
- Baroreceptors – Juxtaglomerular apparatus
- GFR- feedback from distal nephron
- Other

Response
- Hormones – PTH, ANF- decrease NaCl absorption
- Angiotensin, aldosterone, ADH- increase Na Cl absorption
Normal Potassium Balance

- **Intake**
- **Plasma K**
  - Glucagon
  - Insulin
  - Aldosterone
  - High plasma K
- **Renal excretion**
- **Cell K**
Acid-Base Regulation

- pH - negative log of H+ concentration - high pH = low H+, low pH = high H+
- Narrow pH range compatible with life – 6.9-7.6
- Body buffers – HC03, carbonic acid buffers critical – regulated by lung, kidney
- Lung – can get rid of CO2/carbonic acid – controls pH by changing respiratory rate (fast rate – lose CO2/acid, pH rises, etc)
- Kidney – controls pH by differential reabsorption of HCO3 in proximal tubule (low pH leads to more HCO3 reabsorption, etc) AND can trap some H+ in urine as NH4+ distally
NORMAL TUBULOINTERSTITIUM - PAS STAIN
The tubulo-interstitium

What can go wrong?
- Abnormal reabsorption
- Electrolyte abnormalities
- Acid-base problems
- Loss of normal filtration

Causes of injury/disease
- Trauma/physical insults (eg radiation)
- Ischemia- need oxygen!
- Infection – direct or indirect (inflammation)
- Immune diseases- eg lupus (inflammation)-
- Toxins- mushrooms, many drugs
- Metabolism/endocrine
- Congenital/genetic- defects in channels, porters; cystic diseases
- Neoplasia
TUBULAR INJURY WITH LOSS OF POLARIZATION
SCHEMA - TUBULAR EPITHELIAL INJURY AND REPAIR

Sublethally injured cells

Migrating spreading cells

Cell proliferation

Basement membrane
DRUG-INDUCED AIN WITH EOSINOPHILS
POLAR SCARS - VESICOURETERAL REFLUX
CAST WITH LEUKOCYTES, BACTERIA IN URINE
The kidney - vessels

- Graduated in size from the renal artery, which arises from the abdominal aorta, through major renal artery branches, interlobar arteries to intralobular to arcuate to interlobular to intralobular to arterioles to capillaries

- Diseases/injury – due to atherosclerosis, emboli/thrombosis, infection/arteritis, circulating factors/toxins (eg E Coli toxin-hemolytic uremic syndrome)

- Results – ischemia, fibrosis/scarring
Arteriolar Hyalinosis
Arteriosclerosis - Hypertensive
The Kidney - Functions

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Questions?