Urinary System Lecture Hand-out

Reading assignment: Chapter 20: Urinary system (Ross & Pawlina); pay special attention to Folders 20.2, 20.3, 20.4 (Clinical Correlations)

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I. Introduction: Urinary System

Components

The urinary system is comprised of the bilateral kidneys and ureters and a midline urinary bladder and urethra.

The kidneys are glandular organs that produce an ultrafiltrate called urine which is transported by the ureters (muscular tubes) to the urinary bladder for storage. The urine is expelled to the external environment via the urethra.

Urine is produced in a two step process: First, body fluid from the blood stream is collected via filtration through a loosely selective permeable membrane. Hydrostatic (blood) pressure forces water and small solutes (salts, sugars, amino acids, nitrogenous waste) through the membrane while cells and large molecules are retained in the circulatory system. The fluid which passes through the filter is called a filtrate. The second step is the selective re-absorption and secretion of solutes. Active transport is used to selectively re-reabsorb valuable solutes such as glucose, certain salts and amino acids from the filtrate and return them to the circulatory system. Conversely, unfiltered, large molecular wastes are actively
secreted from the circulatory system into the filtrate. The filtrate is then concentrated (actively and passively) and expelled as an ultrafiltrate (urine)

Functions

The urinary system serves a number of functions: (1) It removes metabolic waste (primarily nitrogenous waste from the breakdown of proteins and nucleic acids); (2) it regulates the body's water and solute (electrolyte) composition including pH (osmoregulation); and (3) it has important endocrine functions which include the following:

a. Erythropoietin is produced and secreted by the kidney to regulate erythropoietic cells in the blood marrow.

b. Renin is part of the renin-angiotensin-aldosterone system which controls blood pressure and volume; renin is released from the kidney to the blood circulatory system where it cleaves circulating angiotensinogen to release angiotensin I (see below).

c. Vitamin D: part of the synthetic pathway of this hormone occurs in the kidney

Development

The urinary and genital systems are closely tied through development which explains their use of common excretory ducts (at least in about half of us). Both systems originate from intermediate mesoderm which gives rise to the urogenital ridge from which the two organ systems emerge. This common origin will be further explored in our study of the reproductive systems.

II. Gross structure of the kidney

The kidney is an encapsulated bean-shaped organ. The hilum is a depression on the medial surface that serves as the portal for the renal vessels, nerves and ureter. The renal sinus is the cavity deep to hilum that is occupied by the renal pelvis and vessels. The renal pelvis (L, basin) is simply an expansion of the ureter which receives urine from the major calyces.

The capsule of the kidney in humans is bi-laminar, consisting of an outer layer of dense connective tissue and an inner layer of myofibroblasts. The function of this muscular inner layer is unclear.

Cortex

The parenchyma (distinguishing cells) of the kidney is divisible into (1) cortex and (2) medulla.

The cortex (outer region) is grossly divisible into alternating medullary rays and cortical labyrinths. The medullary rays are rich in straight tubules and collecting ducts; the cortical labyrinths are rich in renal corpuscles, convoluted tubules and collecting tubules. The alternating arrangement of medullary rays and cortical labyrinths gives the kidney its striated appearance in gross section.

Medulla

In organisms with multi-lobate kidneys, such as humans, the medulla (inner region) is divisible into alternating pyramids and renal columns. Renal columns are simply extensions of the cortex into the medullary region and their composition is the same as the cortex. The renal pyramids are variable in number and contain straight tubules (thick and thin), collecting ducts and vasa recta. The apex of each pyramid terminates in a papilla (L., nipple). The papilla is perforated by numerous openings of the terminal collecting ducts and its surface is described as the area cribosa (L, sieve).

The tubular composition of a medullary pyramid varies between its inner and outer portions. In the outer portion (adjacent to the cortex) thick tubules predominate; conversely, in the inner portion thin tubules are more commonly found.
Each pyramid drains at its papillae into a minor calyx; several minor calyces unite to form a major calyx. In turn, major calyces unite to form the renal pelvis which is drained by ureter. [Think of a water shed fed by individual springs; each spring (papilla) feeds a creek (minor calyx); several creek join/flow together to form a river (major calyx) which flows into a lake (renal pelvis); the lake is fed by several rivers (major calyces) each formed by their own set of creeks (minor calyces) and springs (papillae); the lake itself drains to the ocean (urinary bladder) via another river (the ureter). Great! All this talk of flowing water has given me an urge!]

Kidney Lobes and Lobules

A lobe consists of a renal pyramid and its associated (i.e. functionally connected) cortical tissue (adjacent cortex and renal columns). A lobule is a subdivision of a lobe consisting of a central medullary ray and its surrounding cortical material. These divisions are useful for understanding the arterial nomenclature of the kidney (see below).

IV. Nephron – functional unit of kidney

Recall that urine formation is a 2-step process: (1) filtration which occurs in the renal corpuscle and (2) selective re-absorption and secretion which occurs along the length of the renal tubules and collecting ducts.

The nephron is the functional unit of the kidney. It consists of (1) a renal corpuscle (filtration) and renal tubule (selective resorption and secretion). The tubule is U-shaped and sequentially divided into morphological divisions that perform different functions. Starting from the renal corpuscle, these divisions are [potentially] the proximal convoluted tubule, proximal straight tubule, thin descending limb; thin ascending limb, distal straight tubule and distal convoluted tubule. The nephronic loop (loop of Henle) is variably formed by the proximal straight tubule, thin descending limb, thin ascending limb and/or distal straight tubule. Here’s the important point: The composition of the tubule in terms of its divisions and the division which forms its loop varies between the three types of nephrons.

There are 3 different types of nephrons which differ in their composition of the nephronic loop (= loop of Henle):

1. Cortical (sub-capsular) nephrons are the most common type of nephron. Their renal corpuscles are found in the outer cortex and their short loops are formed by distal straight tubules in the outer medulla. Note that these nephrons lack a thin ascending limb (see text Figure 20.3).

2. Juxtamedullary nephrons account for approximately 20% of all nephrons; their corpuscles are found adjacent to the medulla. They are long looped nephrons whose loop is formed by thin limbs in the inner medulla. These nephrons are responsible for producing the urine-concentrating mechanism of the kidney.

3. Intermediate nephrons have their renal corpuscles in the mid-region of the cortex and their loops are intermediate in length.

Renal Corpuscle – site of filtration

Structurally, a renal corpuscle (~ 200 micrometers diameter) consists of a tuft of capillaries called the glomerulus within an epithelial glomerular (Bowman’s) capsule. The capillaries of the glomerulus are fed by an afferent arteriole and drained by an efferent arteriole at the vascular pole. The glomerular capsule is bi-laminar consisting of a visceral layer composed of podocytes and mesangial cells that cover the glomerulus and a parietal layer of simple squamous epithelium which forms the perimeter of the corpuscle. Between the parietal and visceral layers is the urinary space (Bowman’s space) which opens to a proximal convoluted tubule at the urinary pole.

The renal corpuscle forms the filtering apparatus of the nephron; this apparatus is comprised of 3 components: (1) The endothelium of the glomerular capillaries which is highly fenestrated without diaphragms; (2) the glomerular basement membrane which is a thick basal lamina produced by both the
endothelial cells and podocytes; and (3) the visceral layer of the glomerular (Bowman’s) capsule comprised of podocytes and mesangial cells. The podocytes possess processes called pedicles (what alliteration!) that wrap around the capillaries and interdigitate to form filtration slits approximately 25nm wide. The mesangial cells serve a phagocytic function and keep the basement membrane clear of debris. All 3 components combine to retain cells and macromolecules (proteins > 70 kd) within the capillary lumen but permit the passage of water and small solutes (salts, glucose, amino acids, nitrogenous wastes) into the urinary space as filtrate.

Renal tubule – site of selective re-absorption / secretion of solutes

The renal tubule, a simple epithelial tube, serves (1) to recover water and other desirable solutes (sugar, ions, small proteins) from the filtrate and (2) to transport undesirable solutes too large to pass through the corpuscular sieve into the filtrate. The different portions of the renal tubule differ in their function and will be examined from proximal to distal.

The proximal convoluted tubule receives filtrate from the urinary space and is the site of the selective re-absorption of most solutes including all the glucose and amino acids and most of the water and salts. Proteins are absorbed by pinocytosis, broken down by lysosomal degradation and released as amino acids to the peritubular capillary network. This is also the site of pH balancing and elimination (active transport) of creatine.

Structurally the proximal convoluted tubule is formed by a simple cuboidal to low columnar epithelium. The apical surface is covered with microvilli creating a light microscopic brush border that increases the surface area for absorption. The cells are tightly bound to one another to seal off the intercellular spaces from the lumen using junctional processes apically and interdigitating plicae (folds) laterally. Basally, interdigitating processes contain numerous mitochondria which create light microscopic basal striations that are associated with ion transport.

Histologically proximal convoluted tubules are the most abundant tubule in the cortex. They have an eosinophilic cytoplasm with a basal nucleus. The brush border is rarely preserved and the indistinct cells margins are due to basal and lateral border interdigitations.

The proximal straight tubules are located within both the medulla and cortex. They are formed by a lower cuboidal epithelium and their microvilli and basal and lateral interdigitations are less well developed. Histologically they are similar to proximal convoluted tubules.

Descending thin tubules are located within the medulla and are formed by low cuboidal to squamous epithelium. The microvilli are poorly developed as are the basal and lateral interdigitations creating a very leaky cell that serves as the site of passive transport of ions (inward) and water (outward) between the lumen and interstitium.

The ascending thin tubules are also located within the medulla and are similar in appearance to descending thin tubules. However, these tubes are impermeable to water but permit passive transport of NaCl into the interstitium. Cortical nephrons typically lack these segments.

Distal straight tubules are located within both the medulla and cortex. Histologically these appear as a simple cuboidal epithelium with sparse microvilli and lacking lateral interdigitations. The nucleus is apical and basal interdigitations with abundant mitochondria are present. These tubes are impermeable to water and are the site of ion transport from the lumen to the interstitium that establishes the ion gradient of medullary interstitium.

The distal tubule is divisible into 3 parts: straight, macula and convoluted. The macular portion is formed by the macula densa which is where the distal tubule contacts the renal corpuscle. The macula densa is part of the juxtaglomerular apparatus (see below).
Distal convoluted tubules are located within the cortex distal to the macula densa. They are approximately a third (1/3) as long as their proximal counterparts. Histologically they are similar to the distal straight tubules and also function in ion exchange.

IV. Collecting tubules / ducts

The collecting system starts in the cortex as a continuation of the distal convoluted tubules and descends through the medulla. As the ducts coalesce and increase in size, the cells of the tubes change from somewhat squamous to cuboidal to columnar and similarly become increasing stratified. They terminate at the tip of the renal pyramid as the papillary ducts. Histologically they appear as tubes with distinguishable cells margins, central nuclei and poorly staining cytoplasm. At the EM level many posses a single cilium and sparse microvilli. The collecting system functions to concentrate urine through ADH-regulated and ADH-independent water channels.

V. Juxtaglomerular apparatus

The juxtaglomerular apparatus (JGA) is the site of blood pressure regulation via the renin-angioensin-aldosterone system. A JGA is located at the vascular pole of every glomerular (Bowman’s) capsule and is formed by the conjunction of cells of (1) the macula densa (distal tubule) (2) juxtaglomerular cells of the afferent arteriole, and (3) extraglomerular mesangial cells.

The macula densa is the portion of the distal tubule adjacent to the renal corpuscle. These cells monitor the Na+ concentration in the tubular fluid (filtrate) and regulate via paracrine signals the release of renin by the adjacent juxtaglomerular cells. The juxtaglomerular cells are specialized smooth muscle cells in the wall of the afferent arteriole which synthesize and secrete renin. The role the extraglomerular mesangial cells play in this complex is unclear.

How does it work? Here we go: The macula densa cells monitor Na+ levels in the distal tubule filtrate; low levels of filtrate Na+ cause the macula densa cells to secret a paracrine signals that cause the adjacent juxtaglomerular cells to release renin into the afferent arteriole. Renin is a protease that cleaves plasma angiotensinogen into angiotensin I. In the lung, angiotensin I is converted to angiotensin II (by an enzyme present in the pulmonary capillaries). Angiotensin II promotes (1) vascular smooth muscle contraction (raising blood pressure) and (2) release of aldosterone from the suprarenal cortex whose affects increase blood volume and further raise blood pressure.

VI. Interstitium

The interstitium is the connective tissue matrix of the kidney. [Yes, it is the stroma of the kidney, but remember not all stromas are connective tissue.] It is sparse in the cortex and most abundant the deep medulla. The extracellular matrix consists of collagen fibers and glycosamionglycans (GAGs) and the cells are fibroblasts and macrophages.

VII. Blood and nerve supply

Remembering the rule that arterial names are usually toponymic, let’s follow the flow of blood through the kidney:

Arterial: renal artery > inter-lobar arteries > arcuate arteries > inter-lobular arteries > afferent arterioles > renal corpuscle (capillaries!) > efferent arteriole > peritubular capillary network (for cortical nephrons) --or-- > vasa recta (for juxtamedullary nephrons).

Venous: Peritubular capillary network > interlobular veins > arcuate veins > interlobar veins > renal vein.
The vasa recta (L. straight vessels) are comprised of arteriolae rectae and venulae rectae and their associated capillaries. They are important in maintaining (but not creating) the ion gradient of the medullary interstitium established by the nephronic loops (see below). The arteriolae rectae is a direct continuation of the efferent arteriole and the vasa recta follows along the same nephronic loop from which the efferent arteriole exited, thus maintaining the osmotic gradient of the interstitium. The capillaries of the vasa recta are made of thin, fenestrated (leaky) endothelial cells.

Nerve Supply

The smooth muscle of the glomerular arterioles receives sympathetic innervation. Vasoconstriction of afferent arteriole decreases filtration rate (lowers pressure) whereas vasoconstriction of the efferent arterioles increases filtration rate. Neither innervation is necessary for normal renal function. [What experiment conducted tens of thousands a time each year demonstrates this?]

VIII. Structure / Function: How hyperosmotic urine (120 mosm/ L) is produced

The nephronic loop (of Henle) of the juxtamedullary nephrons creates an osmotic gradient in interstitium of medulla, grading from low osmolarity (400 mosm/L) in the outer medulla to high osmolarity (1200 mosm/L) in the inner medulla. The most important component of the loop is the thick ascending limb where active transport of solutes into the interstitium occurs which establishes the osmotic gradient. The vasa recta maintains the osmotic gradient by its counter-current flow thru medulla. The collecting duct is the site of osmotic concentration; modulated by ADH secreted by the hypophysis: ADH increases the water permeability of collecting duct cells allowing water into the interstitium and back into blood via vasa recta resulting in a more concentrated urine.
IX. Ureter / Bladder:

The histological structure of the calyces, renal pelvis, ureter and urinary bladder is broadly similar and each consists of a lumen surrounded by a wall of three coats (tunics): Mucosa, muscularis and adventitia/serosa. The mucosa is lined by transitional epithelium over a lamina propria of irregular connective tissue. The transitional epithelium is impermeable to water and salts. The muscularis is a bilaminar smooth muscle layer with inner longitudinal and outer circular bundles (but see urinary bladder, below). It produces peristalsis to move the urine. The adventitia is the outer connective tissue coat. If it is covered with peritoneum (mesothelium) it is referred to as serosa.

The ureters are muscular tubes connecting the renal pelvis to the urinary bladder.

The urinary bladder (vesica urinaria) is a distensible reservoir. It receives the bilateral ureters and empties via the midline urethra. The muscularis layer forms a detrusor muscle and is formed by smooth muscle bundles arranged in a complex meshwork characteristic of all expelling organs. At the distal end of the bladder, the muscularis is thickened to form the internal urethral sphincter.

X. Urethra

The urethra is a fibromuscular tube connecting the bladder to the external urethral orifice. It is sexually dimorphic. In the males it is the terminal duct for both the urinary and genital systems. In the
female it empties only the bladder. In both sexes the lining grades from a transitional epithelium adjacent to the bladder to a stratified squamous epithelium at the orifice. Males often have a stratified columnar or pseudostratified columnar epithelium in the middle portion.

XI. **Urine plumbing** (courtesy of DRS)

urinary space of glomerular (Bowman's) capsule (neonatal or just born urine) > convoluted proximal tubule (infantile urine) > descending, thick, straight, proximal tubule (toddlerish urine) > descending, thin, straight, proximal tubule (childish urine) > ascending, thin, straight proximal tubule (pre-pubescentish urine) > ascending, thick, straight, distal tubule (pubescentish urine) > convoluted, distal tubule (post-pubescentish urine) > collecting tubule (Gen Xish urine) > collecting ducts (midlife urine) > papillary ducts of Bellini (old fart urine) > minor calyx > major calyx > renal pelvis > ureter > bladder > urethra > outside (in the grave urine)