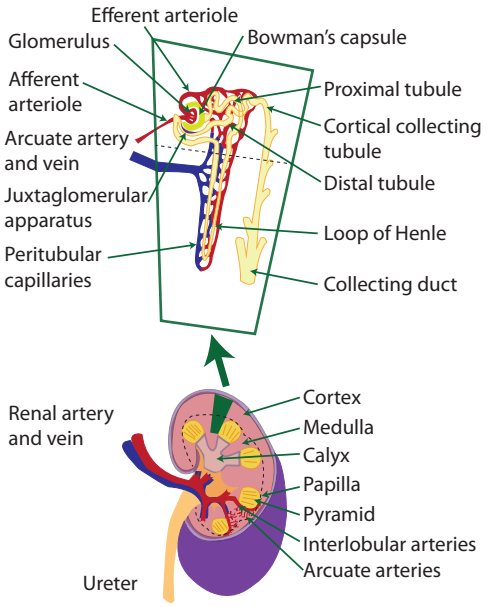
# RENAL PHYSIOLOGY 1

**Functional renal anatomy** Each kidney weighs about 150-200g and is located retroperitoneally just below the diaphram. The renal artery originates from the aorta to supply each kidney. If the kidney is bisected from top to bottom, the two major regions that can be visualized are the outer cortex and the inner region referred to as the medulla. The medulla is divided into multiple cone-shaped masses of tissue called renal pyramids. The base of each pyramid originates at the border between the cortex and medulla and terminates in the papilla, which projects into the space of the renal pelvis, a funnel-shaped continuation of the upper end of the ureter. There are one million nephrons in each kidney. This includes both cortical nephrons which exist out to the periphery (cortex) and the juxtamedullary nephrons which have are able to create a greater osmolality gradient due to their longer length. The nephron is made up of a single layer of epithelial cells separated by a basement membrane. The glomerulus invaginates Bowman's capsule. Fluid is filtered from the glomerular capillaries into Bowman's space under the action of opposing hydrostatic and oncotic pressures. They are supplied by the afferent arteriole and drained by the efferent. The filtration barrier to the movement of fluid and solutes into Bowman's space comprises of the capillary epithelium, a layer of basement membrane, and the capsular endothelial cells, the podocytes. The proximal tubule collects the large volume of the filtrate from Bowman's capsule and reabsorbs 60% of it back into the blood stream. The proximal tubule reabsorbs water, sodium, chloride, potassium, bicarbonate, calcium, glucose, urea, phosphate and any filtered protiens. Substances secreted from the blood into the lumen by the proximal tubule include hydrogen ions, ammonium, urate and organic anions and cations. The loop of Henle consists of a thin limb which descends into the medulla, followed by a hairpin turn and an ascending limb which becomes thick as it passes through the outer medulla on the way to the cortex. The purpose of the loop is to create an increasing interstitual osmotic gradient in the medulla, permitting reabsorption of water from the from the collecting ducts and production of a concentrated urine (up to 1400 mOsmol/kg) in the presence of ADH. The descending limb reabsorbs water, the ascending limb reabsorbs sodium, potassium, chloride, and bicarbonate and secretes hydrogen ions. The distal tubule reabsorbs sodium chloride, bicarbonate, and calcium. Potassium and hydrogen ions are secreted ino the lumen. There is no exchange of water. The collecting duct is composed of two types of cells: principle and intercalated cells. Aldosterone stimulates sodium reabsorption and potassium secretion by principle cells of the cortical collecting ducts. ADH increases the permiability of the cortical and medullary collecting ducts to water.



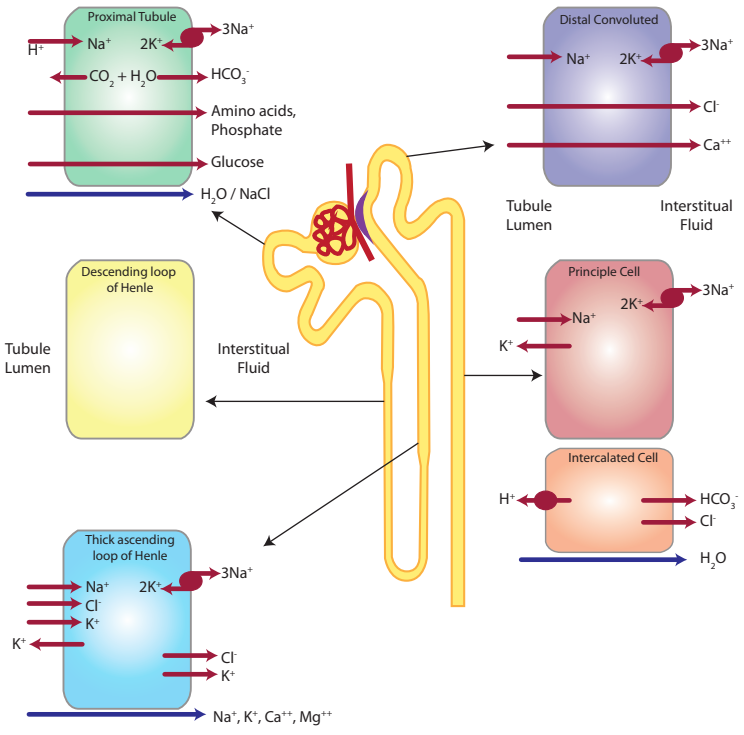

**Renal blood flow** to the two kidneys is normally about 20 per cent of the cardiac output, or 1100 ml/min. Functional anatomy the renal artery enters the kidney through the hilum and then branches progressively to form the interlobar arteries, arcuate arteries, and afferent arterioles, which lead to the glomerular capillaries, where large amounts of fluid and solutes (except the plasma proteins) are filtered to begin urine formation. The renal circulation is unique in that it has two capillary beds, the glomerular and peritubular capillaries, which are arranged in series and separated by the efferent arterioles, which help regulate the hydrostatic pressure in both sets of capillaries. High hydrostatic pressure in the glomerular capillaries (about 60 mm Hg) causes rapid fluid filtration, whereas a much lower hydrostatic pressure in the peritubular capillaries (about 13 mm Hg) permits rapid fluid reabsorption. By adjusting the resistance of the afferent and efferent arterioles, the kidneys can regulate the hydrostatic pressure in both the glomerular and the peritubular capillaries, thereby changing the rate of glomerular filtration, tubular reabsorption, or both in response to body homeostatic demands. The peritubular capillaries empty into the vessels of the venous system, which run parallel to the arteriolar vessels and progressively form the interlobular vein, arcuate vein, interlobar vein, and renal vein, which leaves the kidney beside the renal artery and ureter. Regulation. The main resistors in the kidneys which modify the flow according to different pressures are the efferent and afferent arterioles. Extrinsically there is both neural and hormonal regulation. The kidneys have extensive sympathetic innervation and resistance is increased in response to carotid and aortic body stimulation via the medulla to increase resistance in the afferent and efferent arterioles and reduce flow. The renin angiontensin aldosterone system is also activated in low volume states to retain sodium and water which influences overall flow along with ADH release. Intrisically the kidney demonstrates autoregulation, maintaining a renal blood flow within a systemic pressure range of 75-170 mmHg. The intrinsic control of blood flow is mediated by myogenic stretch mechanisms and tubuloglomerular feedback via afferent ateriole constriction. Tubuloglomerular feedback involves the macula densa which releases adenosine if the renal perfusion pressure rises, and reduces production if the pressure falls. It may also release NO in response to a decreased perfusion pressure. Measurement The clearance of Para Amino Hippuric acid is used to determine renal blood flow, also using an application of the Fick principle. PAH is not utilised or excreted by any other organ apart from the kidney, and once filtered or excreted into the tubules it is not reabsorbed. It has an excretetion ration close to 1.0 therefore the amount excreted is a direct fraction of the plasma filtered (which if the haematocrit is known it can be used to assess renal blood flow).

**Tubule function** the kidneys produce 150-180L of protein free filtrate per day (125ml/min). The tubules process this filtrate by reabsorbing 99% of the Na and H2O, conserving essential nutrients (glucose, amino acids etc) and eliminating potential toxins organic bases and acids, excess K, and exogenous compounds. The primary ATP dependent process in the tubules is the action of the Na.K.ATPase pump. Almost all other transport is via diffusion down gradients or via cotransporters (not shown below). Tubular reabsorption is regulated by physical and hormonal influences. The first is glomerulartubular balance, which simply states that if glomerular filtration increases, reabsorption increases. There is also a net resorptive force which represents the tubular starling forces, and the starling forces of the peritubular capillaries. Tubular function is also under close control of hormonal systems such as the RAAS and parathyroid hormone, and atrial naturetic peptides, and antiduretic hormone.

Proximal tubule - most metabolically active cells in the kidney, high $O_2$ consumption. Reabsorbs 60-70% $Na^+$ and $H_2O$. Complete reabsorption of amino acids and glucose (cotransported with $Na^+$). Almost complete reabsorption of $HCO_3^-$ and excretion of $H^+$ through carbonic anhydrase catalysing the reaction between carbon dioxide and water. Phosphate is also reabsorbed here.

Descending loop of Henle. The cells of the thin descending limb do not carry out active transepithelial ion transport but act as important passive equilibriators in the process of countercurrent multiplication.

Thick ascending loop of Henle is involved in extensive transepithelial reabsorption of $Na^+$ - up to 25% of total, and chloride, with smaller fluxes of $K^+$, $Mg^{++}$ and $Ca^{++}$. It is impermiable to water under all conditions and this allows the countercurrent to be established. This is where loop diuretics (frusemide) work




Distal convoluted tubule is a morphologically and functionally heterogenous segment that extends from the macula densa to the early branching of the CCT. Sodium is reabsorbed with chloride but there is little $K^+$ or $H_2O$ movement. $Ca^{++}$ reabsorption occurs modulated by parathyroid hormone. Thiazides act here and enhance $Ca^{++}$ reabsorption

Cortical collecting duct is the final fine tuning of the urine output. There is reabsorption of some 2-3% of filtered $Na^+$ load, $Cl^-$ reabsorption, $K^+$ (principle cell) and acid excretion (intercalated cell). All of these processes are stimulated by aldosterone. Water permiability is variable and dependent on ADH creating aquaporins. Amiloride and spironolactone act here and cause sparing of potassium and acids.

Christopher Andersen 2012