CONCEPT

GENITOURINARY SYSTEM

Ernawaty Siagian, MSN

Sanksi Pelanggaran Pasal 113
Undang-Undang Nomor 28 tahun 2014
tentang Hak Cipta

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DOTPLUS
Publisher

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Penulis:
Ernawaty Siagian, MSN

ISBN:
978-623-6428-83-2

Editor:
Khairul Azan

Tata Letak:
Hamim Thohari Mahfudhillah

Desain Sampul:
Ananda Ramadhani

Penerbit:

DOTPLUS Publisher
Jln. Penepak RT 12 RW 06, Bengkalis-Riau, 28771
No. Telp/HP: +62 813 2389 9445
Email: redaksidotplus@gmail.com
www.dotpluspublisher.co.id

Cetakan Pertama, Desember 2022
xii + 149 halaman; 15,5 x 23 cm

PREFACE

The kidneys are remarkable organs. Each is smaller than a person's fist, but in a single day the two organs process approximately 1700 L of blood and combine their waste products into approximately 1.5 L of urine. As part of their function, the kidneys filter physiologically essential substances, such as sodium and potassium, from the blood and selectively reabsorb those substances that are needed to maintain the normal composition of internal body fluids. Substances that are not needed or are in excess of those needed pass into the urine. In addition to regulating the volume and composition of body fluids, the kidneys also perform endocrine functions. They release renin, an enzymatic hormone that participates in the regulation of blood pressure and maintenance of the circulating blood volume; they produce erythropoietin, a hormone that stimulates red blood cell production; and they convert vitamin D to its active form.

The genitourinary system is the organ system of the reproductive organs and urinary system. The system plays a very important role in excretory function. Like any other living things, humans strive t maintain balance and homeostatis. This module includes anatomy and physiology, diseases, and drugs. Nursing care for renal problems are also essential to know before taking the exam.

Ernawaty Siagian

“Enjoy the little things in life, for one day you may look back and realize they were the big things.”

- Antonio Smith

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KIDNEY AND URINARY TRACT FUNCTION

1.1 Structure and Function of the Kidney

The primary function of the kidney is to maintain a stable internal environment for optimal cell and tissue metabolism. The kidneys accomplish these life-sustaining tasks by balancing solute and water transport, excreting metabolic waste products, conserving nutrients, and regulating acids and bases. The kidney also has an endocrine function, secreting the hormones renin, erythropoietin, and 1,25-dihydroxy-vitamin D3 for regulation of blood pressure, erythrocyte production, and calcium metabolism, respectively. The kidney also can synthesize glucose from amino acids, performing the process of gluconeogenesis(see What's New? The Kidney and Glucose Regulation). The formation of urine is achieved through the processes of filtration, reabsorption, and secretion by the glomeruli and tubules within the kidney. The bladder stores the urine that it receives from the kidney by way of the ureters. Urine is then removed from the body through the urethra (McCance et al., 2014).

1.2 Functional Anatomy of the Kidney

The kidneys are paired, bean-shaped organs that lie outside the peritoneal cavity in the back of the upper abdomen, one on each side of the vertebral column at the level of the 12 thoracic to 3rd lumbar

vertebrae . The right kidney normally is situated lower than the left, presumably because of the position of the liver. In the adult, each kidney is approximately 10 to 12 cm long, 5 to 6 cm wide, and 2.5 cm deep and weighs approximately 113 to 170 g. The medial border of the kidney is indented by a deep fissure called the hilus. It is here that blood vessels and nerves enter and leave the kidney. The ureters, which connect the kidneys with the bladder, also enter the kidney at the hilus (Port, 2011).

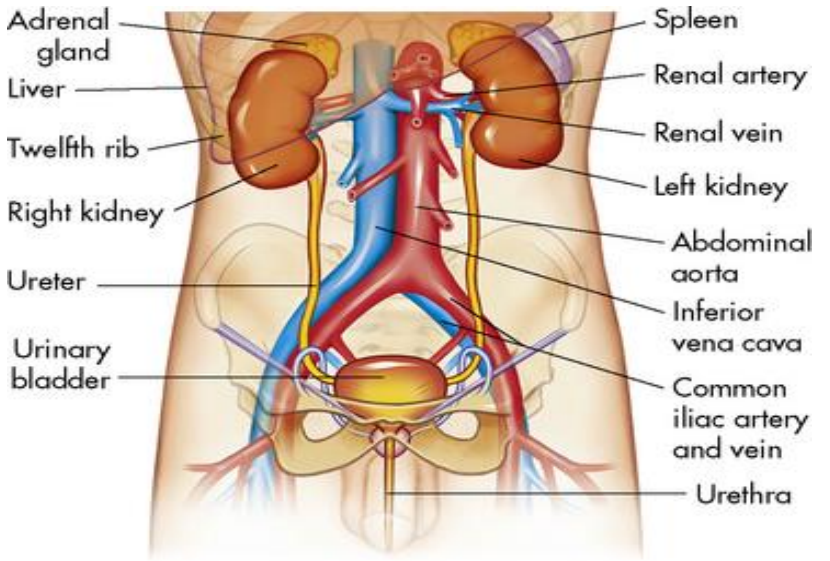


Figure 1.1 Organs of the urinary system

1.3 Gross Structure

The kidney is composed of up to 18 lobes. Each lobular is in turn composed of nephrons, which are the functional units of the kidney. Two distinct regions can be identified on the bisected kidney—an outer cortex and an inner medulla. The cortex has a reddish-brown granular appearance that is absent from the medulla. The medulla consists of light-colored, cone-shaped masses—the

renal pyramids—that are divided by columns of the cortex that extend into the medulla. Each pyramid, topped by a region of cortex, forms a lobe of the kidney. The apices of the pyramids form the papillae (i.e., 8 to 18 per kidney, corresponding to the number of lobes), which are perforated by the openings of the collecting tubules.

The renal pelvis is a wide, funnel-shaped structure at the upper end of the ureter. It is made up of the calyces or cuplike structures that drain the upper and lower halves of the kidney. The kidney is sheathed in a fibrous external capsule and surrounded by a mass of fatty connective tissue, especially at its ends and borders. The adipose tissue protects the kidney from mechanical blows and assists, together with the attached blood vessels and fascia, in holding the kidney in place. Although the kidneys are relatively well protected, they may be bruised by blows to the loin or by compression between the lower ribs and the ileum. Because the kidneys are located outside the peritoneal cavity, injury and rupture do not produce the same threat of peritoneal involvement as that of other organs such as the liver or spleen (Port, 2011).

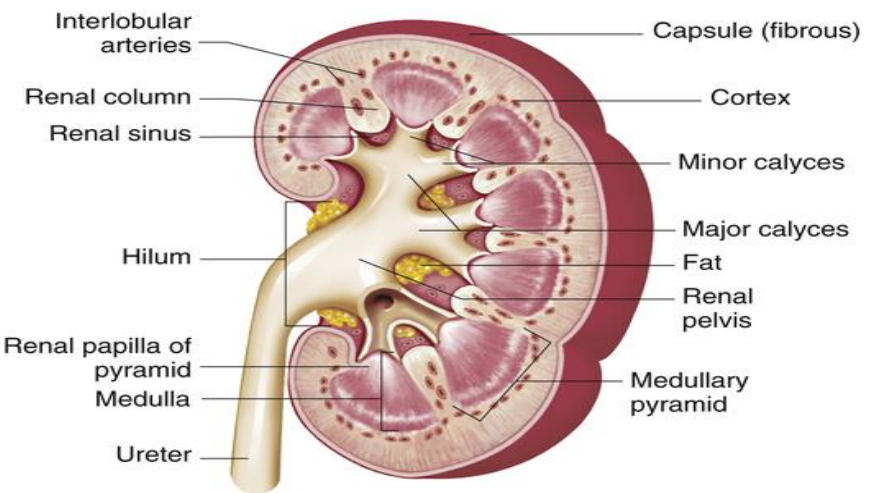


Figure 1.2 Kidney structure

1.4 Renal Blood Supply

Each kidney is supplied by a single renal artery that arises on either side of the aorta. As the renal artery approaches the kidney, it divides into segmental arteries that enter the hilus of the kidney. In the kidney, each segmental artery branches into several lobular arteries that supply the upper, middle, and lower parts of the kidney. The lobular arteries further subdivide to form the interlobular arteries at the level of the corticomedullary junction. These arteries give off branches, the arcuate arteries, which arch across the top of the pyramids. Small intralobular arteries radiate from the arcuate arteries to supply the cortex of the kidney.

The afferent arterioles that supply the glomeruli arise from the intralobular arteries. Although nearly all the blood that enters the kidney flows through the cortex, less than 10% passes into the medulla and only about 1% moves into the papillae. Under conditions of decreased perfusion or increased sympathetic nervous system stimulation, blood flow is redistributed away from the cortex toward the medulla. This redistribution of blood flow decreases glomerular filtration while maintaining the urine-concentrating ability of the kidneys, a factor that is important during conditions such as shock (Port, 2011).

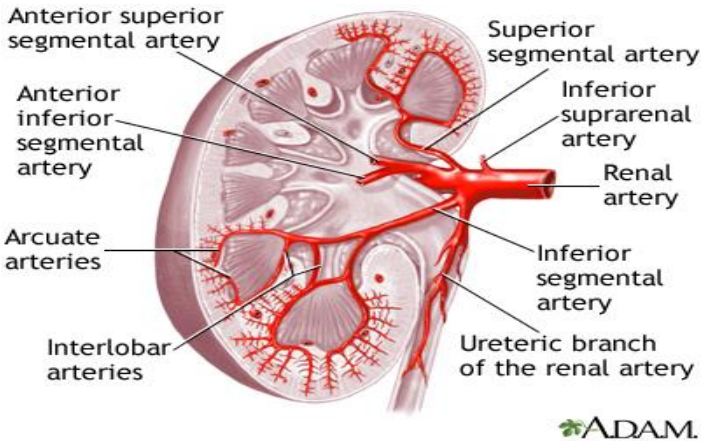


Figure 1.3 Renal blood supply

1.5 The Nephron

Each kidney is composed of more than 1 million tiny, closely packed functional units called nephrons, each of which is capable of producing urine. Each nephron consists of a glomerulus, where blood is filtered, and a system of tubular structures where water, electrolytes, and other substances needed to maintain the constancy of the internal environment are reabsorbed into the bloodstream while other, unneeded materials are secreted into the tubular filtrate for elimination.

Nephrons can be roughly grouped into two categories. Approximately 85% of the nephrons originate in the superficial part of the cortex and are called cortical nephrons. They have short, thick loops of Henle that penetrate only a short distance into the medulla. The remaining 15% are called juxtamedullary nephrons. They originate deeper in the cortex and have longer and thinner loops of Henle that penetrate the entire length of the medulla. The juxtamedullary nephrons are largely concerned with urine concentration. The nephrons are supplied by two capillary systems, the glomerulus and peritubular capillary network.

The glomerulus is a unique, high-pressure capillary filtration system located between two arterioles—the afferent and the efferent arterioles. The peritubular capillaries originate from the efferent arteriole. They are low-pressure vessels that are adapted for reabsorption rather than filtration. These capillaries surround all portions of the tubules, an arrangement that permits rapid movement of solutes and water between the fluid in the tubular lumen and the blood in the capillaries. In the deepest part of the renal cortex, the efferent arterioles continue as long, thin-walled looping vessels called the vasa recta. The vasa recta accompany the long loops of Henle in the medullary portion of the kidney to assist into the exchange of substances flowing in and out of that portion of the kidney. The peritubular capillaries rejoin to form the venous channels through which blood leaves the kidneys and empties into the inferior vena cava (Port, 2011).

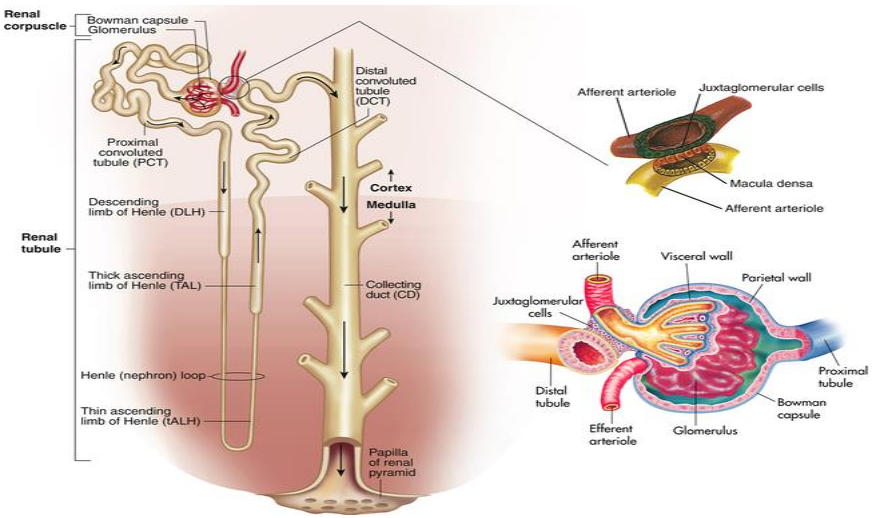


Figure 1.4 Components of the nephron

1.6 The Renal Corpuscle

The renal corpuscle, commonly called the glomerulus, consists of a compact tuft of capillaries, with a central region of mesangial cells and surrounding matrix, encased in a thin double-layered capsule called Bowman capsule. The inner or visceral layer of the capsule envelops the capillaries of the glomerulus and the external or parietal layer forms the outer wall of the capsule. Blood flows into the glomerular capillaries through the afferent arterioles and flows out through the efferent arterioles, which leads to a second capillary network, the peritubular capillaries, that surrounds the renal tubules. Fluid and particles from the blood are filtered through the capillary wall into a fluid-filled space between the visceral and parietal layers of Bowman capsule, called Bowman space. The portion of the blood that is filtered into the capsule space is called the glomerular filtrate.

The glomerular capillary wall consists of a thin layer of endothelial cells, a glomerular basement membrane, and a surrounding layer of visceral epithelial cells of Bowman capsule. The endothelium of the glomerular capillary, which interfaces with blood as it moves through the capillary, contains many small perforations, called fenestrations. These fenestrations allow for the free passage of water, and of small particles such as sodium, potassium, and glucose, but prevent the passage of red blood cells, white blood cells, or platelets. In addition to their role as a filtration barrier, the endothelial cells synthesize a number of vasoactive substances such as nitric oxide (a vasodilator) and endothelin-1 (a vasoconstrictor) that control renal blood flow.

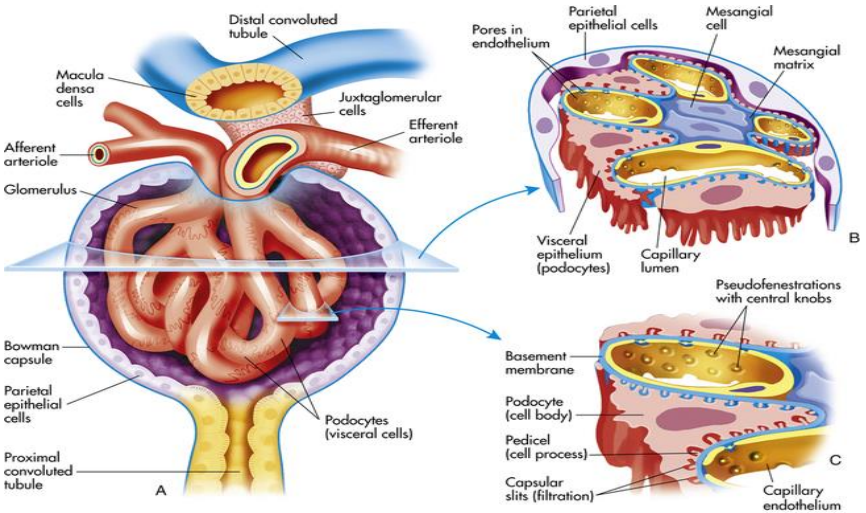


Figure 1.5 Anatomy of The Glomerulus and Juxtaglomerular apparatus

Note:

A, Longitudinal cross section of glomerulus and juxtaglomerular apparatus. **B,** Horizontal cross section of glomerulus. **C,** Enlargement of glomerular capillary filtration membrane.

The glomerular basement membrane consists of a homogeneous acellular meshwork of collagen fibers, glycoproteins, and mucopolysaccharides. Because the endothelial and epithelial layers of the glomerular capillary have porous structures, the basement membrane determines the permeability of the capillary membrane. The spaces between the fibers that make up the basement membrane represent the pores of a filter and determine the size-dependent permeability barrier of the glomerulus. The size of the pores in the basement membrane normally prevents red blood cells and plasma proteins from passing into the filtrate. Alterations in the structure and function of the glomerular basement membrane are

responsible for the leakage of proteins and blood cells into the filtrate that occurs in many forms of glomerular disease.

The visceral layer of the Bowman capsule is composed of epithelial cells that are highly modified to perform a filtering function. These large cells, called podocytes, have numerous finger-like processes that completely encircle the outer surface of the capillaries. The elongated spaces between the interdigitating foot processes, called filtration slits, function as a size-selective filter that prevents proteins and macromolecules that have crossed the basement membrane from entering Bowman space. Another important component of the glomerulus is the mesangium. In some areas, the capillary endothelium and the basement membrane do not completely surround each capillary tuft. Instead, the mesangial cells, which lie between the tufts, provide support for the glomerulus in these areas.

The mesangial cells produce an intercellular substance similar to that of the basement membrane. This substance covers the endothelial cells where they are not covered by basement membrane. The mesangial cells also exhibit contractile properties and are thought to contribute to the regulation of blood flow through the glomerulus; possess phagocytic properties and remove macromolecular materials that enter the intercapillary spaces; and are capable of proliferation. Although the mesangial area is normally narrow and contains only a small number of cells, mesangial hyperplasia and increased mesangial matrix develop in many forms of glomerular disease.

1.7 Tubular Components of the Nephron

The nephron tubule is divided into several segments: the proximal tubule, which drains Bowman capsule; a thin looped structure, the loop of Henle; a distal coiled portion, the distal convoluted tubule; and the final segment, the collecting tubule. The filtrate passes through each of these segments before reaching the pelvis of the kidney. The proximal tubule is a highly coiled structure that lies in the cortex of the kidney and dips toward the renal pelvis to become the loop of Henle.

The loop consists of a descending and ascending limb. The ascending loop of Henle returns to the region of the renal corpuscle, where it becomes much thicker, and is referred to as the thick ascending limb. Beyond the thick ascending limb of Henle is the distal convoluted tubule, which like the proximal tubule lies in the renal cortex. The distal convoluted tubule is divided into two segments: the diluting segment and the late distal tubule. The late distal tubule fuses with the collecting tubule the collecting tubule is divided into two segments: the cortical tubule and the medullary collecting tubule.

The initial parts of 8 or 10 cortical collecting tubules join to form a single large tubule that moves down into the medulla to become the medullary collecting tubule. Throughout its course, the tubule is composed of a single layer of epithelial cells resting on a basement membrane. The structure of the epithelial cells varies with tubular function. The cells of the proximal tubule have a fine, villous structure that increases the surface area for reabsorption; they also are rich in mitochondria, which support active transport processes. The epithelial layer thins in segments of the loop of Henle and has few mitochondria, indicating minimal metabolic activity and reabsorptive function (Port, 2011).

1.8 Urine Formation

Urine formation involves the filtration of blood by the glomerulus to form an ultrafiltrate of urine, the selective reabsorption by the renal tubules of substances needed to maintain the constancy of the internal environment, and the secretion of unneeded and waste materials into the urine filtrate. The urine that is formed represents the sum of the three processes—glomerular filtration, tubular reabsorption, and tubular secretion.

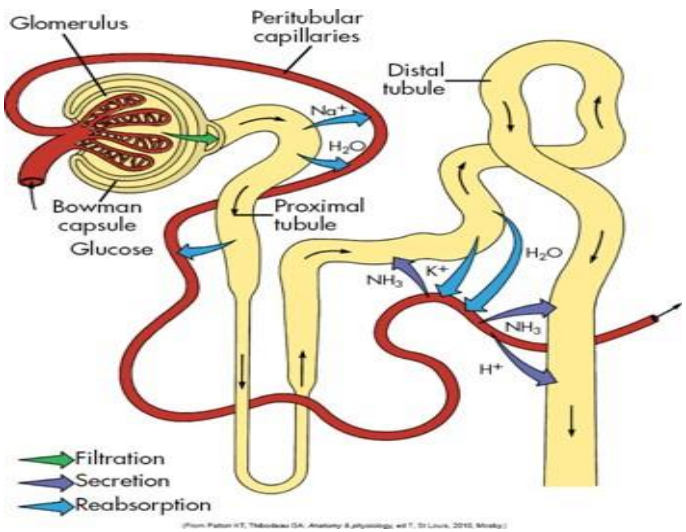


Figure 1.6 Urine formation: Glomerular filtration, Tubular reabsorption, and Tubular secretion

The three processes by which the kidneys excrete urine. Water, electrolytes, glucose, and organic molecules are filtered at the glomerulus. Sodium and glucose are reabsorbed into peritubular capillaries by active transport from the proximal convoluted tubules and water reabsorption follows by osmosis. Sodium is reabsorbed by active transport from distal convoluted tubules; more sodium is conserved when aldosterone is secreted. Osmotic reabsorption of

water from them occurs when ADH is present. Secretion of ammonia (NH3), hydrogen, and potassium occurs from peritubular capillaries into distal tubules by active transport (Patton & Thibodeau, 2013).

1.9 Glomerular Filtration

Urine formation begins with the filtration of essentially protein-free plasma through the glomerular capillaries into the Bowman space. The movement of fluid through the glomerular capillaries is determined by the same factors (i.e., capillary filtration pressure, colloidal osmotic pressure, and capillary permeability) that affect fluid movement through other capillaries in the body. The glomerular filtrate has a chemical composition similar to plasma, but contains almost no proteins because large molecules do not readily pass through the openings in the glomerular capillary wall. Approximately 125 mL of filtrate is formed each minute. This is called the glomerular filtration rate (GFR). This rate can vary from a few milliliters per minute to as high as 200 mL/minute. The location of the glomerulus between two arterioles allows for maintenance of a high-pressure filtration system. The capillary filtration pressure (approximately 60 mm Hg) in the glomerulus is approximately two to three times higher than that of other capillary beds in the body.

The filtration pressure and the GFR are regulated by relaxation and constriction of the afferent and efferent arterioles. For example, relaxation of the afferent arteriole increases the filtration pressure and the GFR by increasing glomerular blood flow; whereas relaxation of the efferent arteriole decreases resistance to outflow of blood, decreasing the glomerular pressure and the GFR. The afferent and the efferent arterioles are innervated by the sympathetic nervous system and are sensitive to vasoactive hormones, such as angiotensin II. During periods of strong sympathetic stimulation, such as shock,

constriction of the afferent arteriole causes a marked decrease in renal blood flow, and thus glomerular filtration pressure. Consequently, urine output can fall almost to zero (Port, 2011).

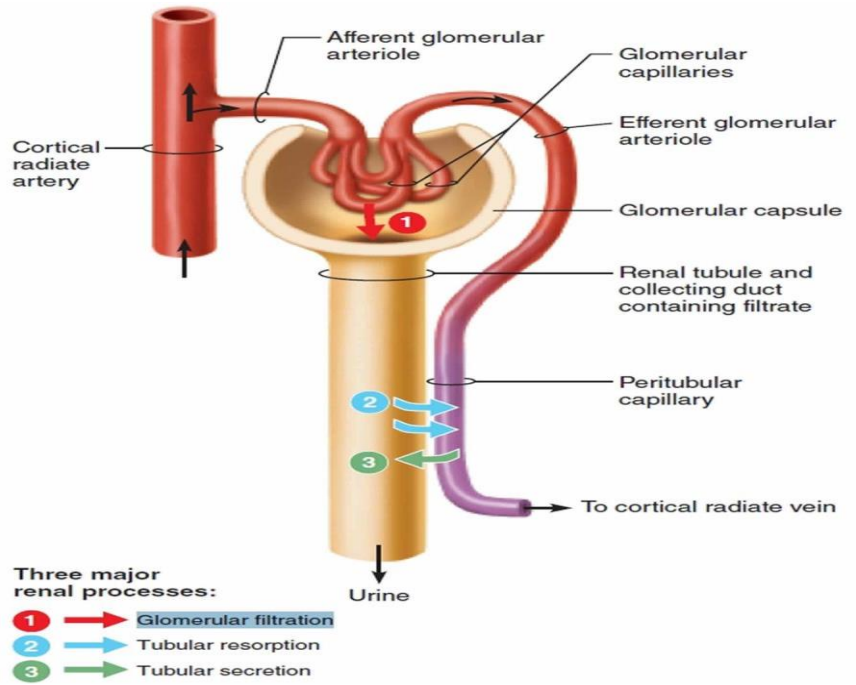


Figure 1.7 Glomerular filtration process

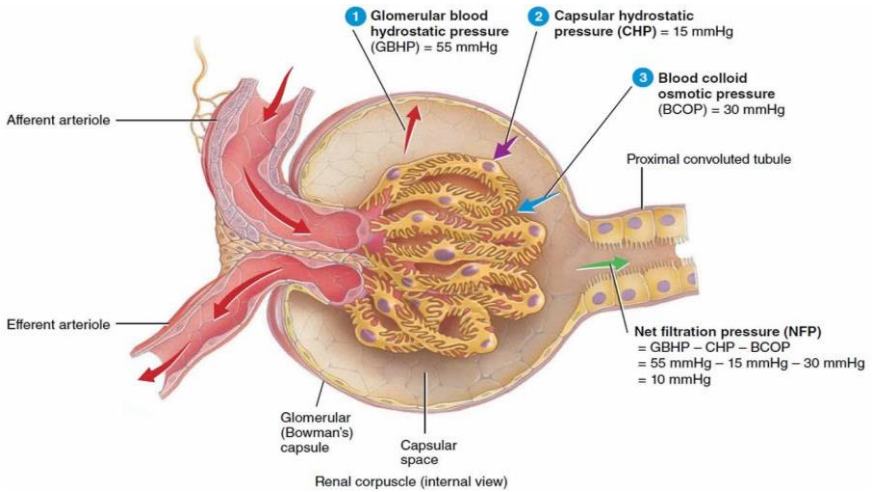


Figure 1.8 Glomerular filtration pressure

1.10 Tubular Reabsorption and Secretion

From Bowman capsule, the glomerular filtrate moves into the tubular segments of the nephron. In its movement through the lumen of the tubular segments, the glomerular filtrate is changed considerably by the tubular transport of water and solutes. Tubular transport can result in reabsorption of substances from the tubular fluid into the peritubular capillaries or secretion of substances into the tubular fluid from the blood in the peritubular capillaries. The mechanisms of transport across the tubular cell membrane are similar to those of other cell membranes in the body and include active and passive transport mechanisms. Water and urea (a by-product of protein metabolism) are passively absorbed along concentration gradients. Sodium (Na+), other electrolytes, as well as urate (a metabolic end-product of purine metabolism), glucose, and amino acids, are reabsorbed using primary or secondary active transport mechanisms to move across the tubular membrane. Some substances, such excess K+ and urate, are secreted into the tubular

fluids. Under normal conditions, approximately 1 mL of the 125 mL of glomerular filtrate that is formed each minute is excreted in the urine. The other 124 mL is reabsorbed in the tubules. This means that the average output of urine is approximately 60 mL/hour. Renal tubular cells have two membrane surfaces through which substances must pass as they are reabsorbed from the tubular fluid.

The outside membrane that lies adjacent to the interstitial fluid is called the basolateral membrane, and the side that is in contact with the tubular lumen and tubular filtrate is called the luminal membrane. In most cases, substances move from the tubular filtrate through the luminal membrane into the tubular cell along a concentration gradient, but they require facilitated transport or carrier systems to move across the basolateral membrane into the interstitial fluid, where they are absorbed into the peritubular capillaries.

The bulk of energy used by the kidney is for active sodium transport mechanisms that facilitate sodium reabsorption and cotransport of other electrolytes and substances such as glucose and amino acids. This is called secondary active transport or cotransport. In secondary active transport, two or more substances interact with a specific membrane protein (a carrier protein) and are transported across the membrane. As one of the substances (in this case sodium) diffuses down its concentration gradient, the energy released is used to move another substance (for instance, glucose or an amino acid) against its concentration gradient. Thus, the secondary active transport of a substance such as glucose does not require energy directly from adenosine triphosphatase (ATPase), but depends on the energy-dependent Na^+/K^+-adenosine triphosphatase (ATPase) pump on the basolateral side of renal tubular cells. This pump maintains a low intracellular sodium concentration that facilitates the downhill movement of sodium across the luminal membrane; it is

this downhill diffusion of sodium to the interior of the cell that provides the energy for the simultaneous uphill transport of glucose across the luminal membrane. A few substances, such as hydrogen (H+), are secreted into the tubule.

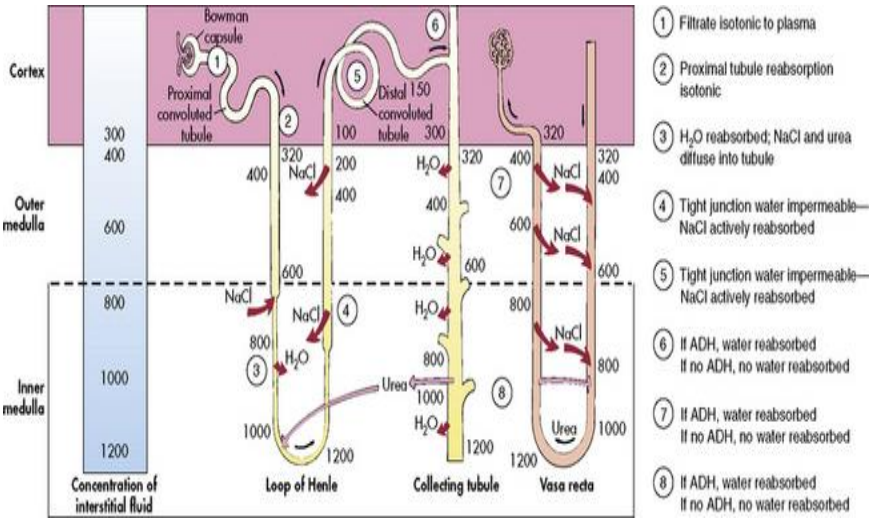


Figure 1.9 Countercurrent mechanism for concentrating and Diluting urine. ADH, Antidiuretic hormone
(*Note*: Numbers in illustration represent milliosmoles).

1.11 Proximal Tubule

Approximately 65% of all reabsorptive and secretory processes that occur in the tubular system take place in the proximal tubule. There is almost complete reabsorption of nutritionally important substances, such as glucose, amino acids, lactate, and water-soluble vitamins. Electrolytes, such as Na^+, K^+, Cl^-, and bicarbonate (HCO^{3-}), are 65% to 80% reabsorbed. As these solutes move into the tubular cells, their concentration in the tubular lumen decreases, providing a concentration gradient for the osmotic reabsorption of water and urea. The proximal tubule is highly

permeable to water, and the osmotic movement of water occurs so rapidly that the concentration difference of solutes on either side of the membrane seldom is more than a few milliosmoles. Many substances, such as glucose, are freely filtered in the glomerulus and reabsorbed by energy-dependent cotransport carrier mechanisms. The maximum amount of substance that these transport systems can reabsorb per unit time is called the transport maximum.

The transport maximum is related to the number of carrier proteins that are available for transport and usually is sufficient to ensure that all of a filtered substance such as glucose can be reabsorbed rather than being eliminated in the urine. The plasma level at which the substance appears in the urine is called the renal threshold. Under some circumstances, the amount of substance filtered in the glomerulus exceeds the transport maximum. For example, when the blood glucose level is elevated in uncontrolled diabetes mellitus, the amount that is filtered in the glomerulus often exceeds the transport maximum (approximately 320 mg/minute), and glucose spills into the urine. In addition to reabsorbing solutes and water, cells in the proximal tubule also secrete organic cations and anions into the urine filtrate. Many of these organic anions and cations are end products of metabolism (e.g., urate, oxalate) that circulate in the plasma. The proximal tubule also secretes exogenous organic compounds such as penicillin, aspirin, and morphine. Many of these compounds are bound to plasma proteins and not freely filtered in the glomerulus. Therefore, excretion by filtration alone eliminates only a small portion of these potentially toxic substances from the body.

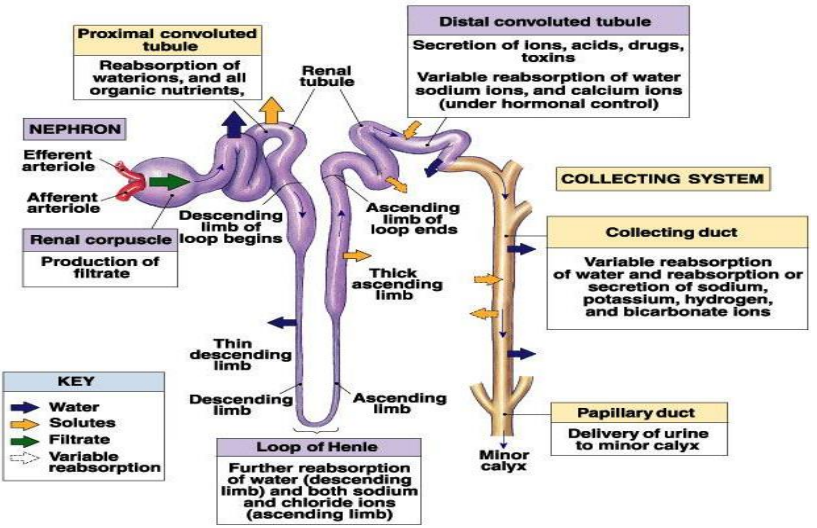
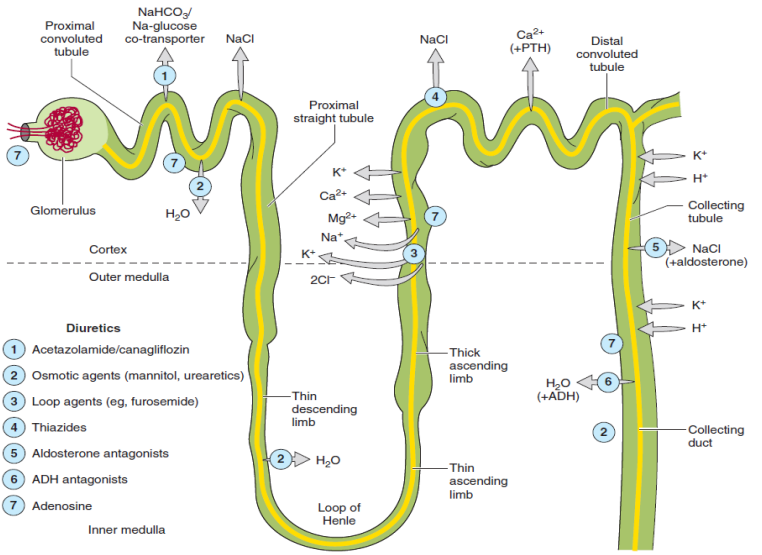


Figure 1.10 Proximal Tube



Tubule transport systems and sites of action of diuretics. ADH, antidiuretic hormone; PTH, parathyroid hormone.

Source : Basic & Clinical Pharmacology 14th Edition

Figure 1.11 Tubule transport system and Sites of action of diuretics, ADH, Antidiuretic hormone, PTH, Parathyroid hormone.

1.12 Loop of Henle

The loop of Henle plays an important role in controlling the concentration of the urine. It does this by establishing a high concentration of osmotically active particles in the interstitium surrounding the medullary collecting tubules where the antidiuretic hormone exerts its effects. The loop of Henle is divided into three segments: the thin descending segment, the thin ascending segment, and the thick ascending segment. Taken as a whole, the loop of Henle always reabsorbs more sodium and chloride than water. This is in contrast to the proximal tubule, which reabsorbs sodium and water in equal proportions. The thin descending limb is highly permeable to water and moderately permeable to urea, sodium, and other ions.

As the urine filtrate moves down the descending limb, water moves out of the filtrate into the surrounding interstitium. Thus, the osmolality of the filtrate reaches its highest point at the elbow of the loop of Henle. In contrast to the descending limb, the ascending limb of the loop of Henle is impermeable to water. In this segment, solutes move out, but water cannot follow and remains in the filtrate. As a result, the tubular filtrate becomes more and more dilute, often reaching an osmolality of 100 mOsm/kg H_2O as it enters the distal convoluted tubule, compared with the 285 mOsm/kg H_2O in plasma. This allows for elimination of free water from the body. For this reason, the segment of the tubule is often called the diluting segment.

The thick segment of the loop of Henle begins in the ascending limb where the epithelial cells become thickened. As with the thin ascending limb, this segment is impermeable to water. The thick segment contains a $Na^+/K^+/2Cl^-$ cotransport system. This system involves the cotransport of positively charged Na^+ and K^+ accompanied by two negatively charged Cl^-. The gradient for the operation of this cotransport system is provided by the basolateral

membrane sodium–potassium ATPase pump, which maintains a low intracellular sodium concentration. Approximately 20% to 25% of the filtered load of sodium, potassium, and chloride is reabsorbed in the thick loop of Henle. Movement of these ions out of the tubule leads to the development of a transmembrane potential that favors the passive reabsorption of small divalent cations such as calcium and magnesium. The thick ascending loop of Henle is the site of the powerful "loop" diuretics (e.g., furosemide [Lasix]), which exert their action by inhibiting the $Na^+/K^+/2Cl^-$cotransporters (Port, 2011).

1.13 Distal and Collecting Tubules.

Like the thick ascending loop of Henle, the distal convoluted tubule is relatively impermeable to water, and reabsorption of sodium chloride from this segment further dilutes the tubular fluid. Sodium reabsorption occurs through a Na^+/Cl^- cotransport mechanism. Approximately 5% of filtered sodium chloride is reabsorbed in this section of the tubule. Unlike the thick ascending loop of Henle, neither Ca^{++} nor Mg^{++} is passively absorbed in this segment of the tubule. Instead, Ca^{++} is actively reabsorbed in a process that is largely regulated by parathyroid hormone and possibly by vitamin D.

The thiazide diuretics, which are widely used to treat disorders such as hypertension, exert their action by blocking sodium reabsorption in this segment of the renal tubules, while enhancing the active reabsorption of calcium into the blood via the calcium-sodium exchange transport mechanism. For this reason, thiazide diuretics have proved useful in reducing the incidence of calcium kidney stones in persons with hypercalciuria. The late distal tubule and the cortical collecting tubule constitute the site where aldosterone exerts its action on sodium reabsorption and potassium secretion and elimination. Although responsible for only 2% to 5%

of sodium chloride reabsorption, this site is largely responsible for determining the final sodium concentration of the urine. The late distal tubule with the cortical collecting tubule also is the major site for regulation of potassium excretion by the kidney.

When the body is confronted with a potassium excess, as occurs with a diet high in potassium content, the amount of potassium secreted into the urine filtrate at this site may exceed the amount filtered in the glomerulus. The mechanism for sodium reabsorption and potassium secretion in this section of the nephron is distinct from other tubular segments. This tubular segment is composed of two types of cells, the intercalated cells and principal cells. The intercalated cells secrete hydrogen (H^+) ions and reabsorb bicarbonate (HCO^{3-}) ions. Thus, they play a key role in acid–base regulation. H^+ secretion by the intercalated cells is mediated by the action of a hydrogen ATPase transporter, in which H^+ are generated by the carbonic anhydrase-mediated reaction, in which water (H_2O) and carbon dioxide (CO_2) combine to form carbonic acid (H_2CO^{3-}), which then dissociates to form H^+ and HCO^{3-}. The H^+ ions are then secreted into the tubular fluid and the HCO^{3-} become available for reabsorption. The principal cells reabsorb sodium and water from the tubule lumen and secrete potassium into the lumen. Sodium reabsorption and potassium secretion depend on the activity of a sodium–potassium ATPase pump located on the basolateral membrane. This pump maintains a low sodium concentration inside the cell by moving sodium down its concentration gradient into the cell through special sodium channels. The pump also establishes a high concentration of potassium within the cell, causing it to diffuse down its concentration gradient across the luminal membrane into the tubular fluid.

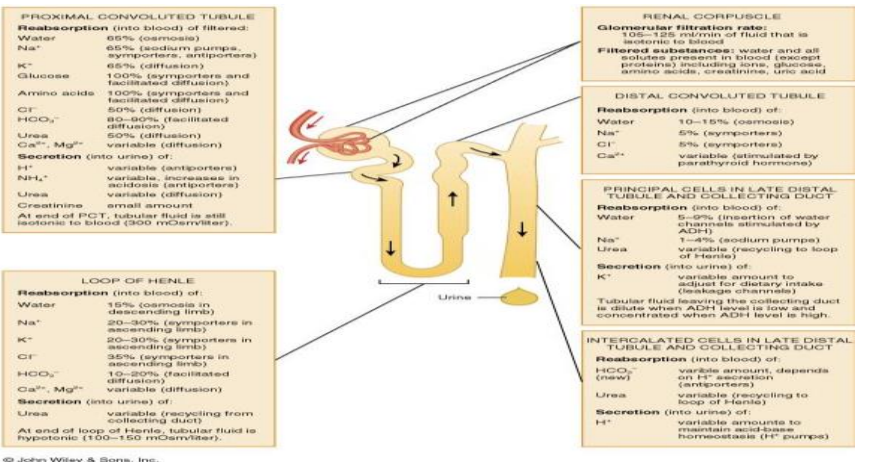


Figure 1.12 Distal and collecting tubules

1.14 Regulation of Urine Concentration

The ability of the kidney to respond to changes in the osmolality of the extracellular fluids by producing either a concentrated or dilute urine depends on the establishment of a high concentration of osmotically active particles in the interstitium of the kidney medulla and the action of the antidiuretic hormone (ADH) in regulating the water permeability of the surrounding medullary collecting tubules (see Understanding How the Kidney Concentrates Urine).In approximately one fifth of the juxtamedullary nephrons, the loops of Henle and vasa recta descend into the medullary portion of the kidney, forming a countercurrent system that controls water and solute movement so that water is kept out of the area surrounding the tubule and solutes are retained. The term countercurrent refers to a flow of fluids in opposite directions in adjacent structures. In this case, there is an exchange of solutes between the adjacent descending and ascending loops of Henle and between the ascending and descending sections of the vasa recta. Because of these exchange processes, a high concentration of osmotically active particles

(approximately 1200 mOsm/kg H_2O) collects in the interstitium of the kidney medulla. The presence of these osmotically active particles in the interstitium surrounding the medullary collecting tubules facilitates the ADH-mediated reabsorption of water.

Antidiuretic hormone assists in the maintenance of the extracellular fluid volume by controlling the permeability of the medullary collecting tubules. Osmoreceptors in the hypothalamus sense an increase in osmolality of extracellular fluids and stimulate the release of ADH from the posterior pituitary gland. In exerting its effect, ADH, also known as vasopressin, binds to receptors on the basolateral side of the tubular cells. Binding of ADH to the vasopressin receptors causes water channels, known as aquaporin-2 channels, to move into the luminal side of the tubular cell membrane, producing a marked increase in water permeability. At the basolateral side of the membrane, water exits the tubular cell into the hyperosmotic interstitium of the medullary area, where it enters the peritubular capillaries for return to the vascular system. The aquaporin-2 channels are thought to have a critical role in inherited and acquired disorders of water reabsorption by the kidney, such as diabetes insipidus (Port, 2011).

1.15 Regulation of Renal Blood Flow and the GFR

In the adult, the kidneys are perfused with 1000 to 1300 mL of blood per minute, or 20% to 25% of the cardiac output. This large blood flow is mainly needed to ensure a sufficient GFR for the removal of waste products from the blood, rather than for the metabolic needs of the kidney. Feedback mechanisms, both intrarenal (e.g., autoregulation, local hormones) and extrarenal (e.g., sympathetic nervous system, blood-borne hormones), normally keep blood flow and the GFR constant despite changes in arterial blood pressure.

1.16 Neural and Humoral Control Mechanisms

The kidney is richly innervated by the sympathetic nervous system. Increased sympathetic activity causesconstriction of the afferent and efferent arterioles and thus a decrease in renal blood flow. Intense sympathetic stimulation such as occurs in shock and trauma can produce marked decreases in renal blood flow and GFR, even causing blood flow to cease altogether. Several humoral substances, including angiotensin II, ADH, and the endothelins, produce vasoconstriction of renal vessels. The endothelins are a group of peptides released from damaged endothelial cells in the kidney and other tissues. Although not thought to be an important regulator of renal blood flow during everyday activities, endothelin I may play a role in the reduction of blood flow in conditions such as postischemic renal failure. Other substances such as dopamine, nitric oxide, and prostaglandins (i.e., E2 and I2) produce vasodilation.

Nitric oxide, a vasodilator produced by the vascular endothelium, appears to be important in preventing excessive vasoconstriction of renal blood vessels and allowing normal excretion of sodium and water. Prostaglandins are a group of mediators of cell function that are produced locally and exert their effects locally. Prostaglandins do not appear to play a major role in regulating renal blood flow and GFR under normal conditions, but may protect the kidneys against the vasoconstricting effects of sympathetic stimulation and angiotensin II. This effect is important because it prevents severe and potentially harmful vasoconstriction and ischemia during conditions such as hemorrhage and shock. Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) that inhibit prostaglandin synthesis may decrease renal blood flow and GFR under certain conditions.

1.17 Autoregulatory Mechanisms

The constancy of blood flow through body tissues is maintained by a process called autoregulation. In most tissues other than the kidneys, autoregulation functions to maintain blood flow at a level consistent with the metabolic needs of the tissues. In the kidney, autoregulation of blood flow also functions to maintain a relatively constant GFR and to allow for the precise regulation of solute and water excretion.

Two major systems are credited with maintaining the constancy of renal blood flow and GFR: one responds to changes in arterial pressure and the other to changes in the sodium chloride concentration in the distal tubular fluid. Both serve to regulate the tone of the afferent arteriole. The pressure sensitive mechanism, termed the myogenic mechanism, relies on the intrinsic property of vascular smooth muscle that causes it to contract when stretched. Thus, when the arterial pressure rises and the afferent arteriole is stretched, the smooth muscle contracts; when arterial pressure falls, the smooth muscle relaxes.

The second mechanism, termed the tubuloglomerular feedback mechanism, involves a feedback loop in which the sodium chloride concentration in the tubular fluid is sensed by the juxtaglomerular apparatus ("juxta" meaning "next to") in the distal tubule. This feedback system, which is located at the site where the distal tubule extends back to the glomerulus and then passes between the afferent and efferent arterioles, includes a group of sodium sensing cells called the macula densa and special secretory cells in the walls of afferent and efferent arterioles called juxtaglomerular cells that synthesize and release the enzyme renin. Because of its location between the afferent and efferent arterioles, the juxtaglomerular apparatus is thought to play an essential feedback

role in linking the level of arterial blood pressure and renal blood flow to the GFR and the composition of the distal tubular fluid. It is thought to monitor the arterial blood pressure by sensing both the stretch of the afferent arteriole and the concentration of sodium chloride in the tubular filtrate as it passes through the macula densa. This information is then used in determining how much renin should be released to keep the arterial blood pressure within its normal range and maintain a relatively constant GFR. A decrease in the GFR, for example, increases sodium chloride reabsorption, thereby decreasing the delivery of sodium chloride to the macula densa.

The decrease in delivery of sodium chloride to the macula densa has two effects: it decreases resistance to blood flow in the afferent arteriole, which raises glomerular filtration pressure; and it increases the release of renin from the juxtaglomerular cells. The renin from these cells functions as an enzyme to convert the plasma protein angiotensinogen to angiotensin I, which is converted to angiotensin II in the lungs. Angiotensin II acts to constrict the efferent arteriole as a means of producing a further increase in the glomerular filtration pressure; thereby returning the GFR toward a more normal range.

1.18 Effects of Increased Protein and Glucose Load

Although renal blood flow and glomerular filtration are relatively stable under most conditions, two factors can increase renal blood flow and glomerular filtration: (1) high protein intake, (2) an increase in blood glucose. With ingestion of a high-protein meal, renal blood flow increases 20% to 30% within 1 to 2 hours. Although the exact mechanism for this increase is uncertain, it is thought to be related to the fact that amino acids and sodium are absorbed together in the proximal tubule via secondary active transport. As a result, delivery of sodium to the macula densa is

decreased, which elicits an increase in renal blood flow through the juxtaglomerular apparatus feedback mechanism. The resultant increase in blood flow and GFR allows sodium excretion to be maintained at a near-normal level while increasing the excretion of the waste products of protein metabolism, such as urea. The same mechanism is thought to explain the large increases in renal blood flow and GFR that occur with high blood glucose levels in persons with uncontrolled diabetes mellitus.

1.19 Elimination and Endocrine Functions of the Kidney

The kidneys play a critical role in maintaining the volume and composition of body fluids through the reabsorption of water and electrolytes, as well as in ridding the body of waste products. The kidneys also have endocrine functions that are important to the regulation of blood pressure, production of red blood cells, and absorption of calcium.

1.20 Elimination Functions of the Kidney

The functions of the kidney focus on elimination of water, excess electrolytes, metabolic acids, and waste products from the blood. As renal function declines, there is an increase in serum levels of substances such as urea, creatinine, phosphate, and potassium.

1.21 Sodium and Potassium Elimination

Elimination of sodium and potassium is regulated by the GFR and by humoral agents that control their reabsorption. Aldosterone, a hormone secreted by the adrenal gland, functions in the regulation of sodium and potassium elimination by the principal cells in the distal and collecting tubules. Sodium reabsorption in the distal and

collecting tubules is highly variable and depends on the presence of aldosterone. In the presence of aldosterone, which stimulates sodium absorption and simultaneous excretion of potassium into the tubular fluid, almost all the sodium in the distal tubular fluid is reabsorbed, and the urine essentially becomes sodium free. In the absence of aldosterone, virtually no sodium is reabsorbed from the distal tubule and excessive amounts of sodium are lost in the urine. The remarkable ability of the distal tubular and collecting duct cells to alter sodium reabsorption in relation to changes in aldosterone allows the kidneys to excrete urine with sodium levels that range from a few tenths of a gram to 40 g/day.

Atrial natriuretic peptide (ANP) is also believed to have an important role in salt and water excretion by the kidney. It is synthesized by muscle cells in the atria of the heart and released when the atria are stretched. Increased levels of this peptide directly inhibit the reabsorption of sodium and water in the renal tubules. Atrial natriuretic peptide also inhibits renin secretion and therefore angiotensin II formation, which in turn reduces reabsorption of sodium. This decreased sodium reabsorption increases urine output and helps return blood volume to normal. Atrial natriuretic peptide levels, which become elevated when the atria are stretched in congestive heart failure, help to decrease vascular volume by increasing urine output. Like sodium, potassium is freely filtered in the glomerulus and reabsorbed in the proximal and distal tubule. Unlike sodium, however, potassium is both reabsorbed from and secreted into the tubular fluid. The amount of potassium that is delivered to the distal tubule each day is only about 70 mEq, yet the average person consumes that much or more in the diet. Therefore, the excess potassium that is not filtered in the glomerulus must be secreted into the tubular fluid so it can be eliminated in the urine. Potassium secretion occurs mainly in the distal and collecting

tubules, with plasma potassium and aldosterone levels being the main physiological regulators of the secretory process. A rise in plasma potassium due to an increase in dietary intake increases potassium secretion and urinary excretion; correspondingly, a fall in plasma levels due to a decrease in dietary intake increases reabsorption and decreases urinary excretion. Aldosterone also exerts a strong influence on potassium secretion in the distal and collecting tubules. In the absence of aldosterone, as occurs in Addison disease, potassium secretion is markedly decreased, causing blood levels to increase.

1.22 Regulation of Body pH

The average North American diet results in the liberation of 40 to 80 mmol of H+ each day. Neither blood buffer systems nor the respiratory control mechanisms for carbon dioxide elimination can eliminate H+ from the body. This is accomplished by the kidneys. Virtually all the excess H+ excreted in the urine are secreted into the tubular fluid by means of tubular secretory mechanisms.

The lowest tubular fluid pH that can be achieved without damaging the kidney structures is about 4.5. The ability of the kidneys to excrete large amounts of H^+ in the urine is accomplished by combining the excess ions with buffers in the urine. The three major urine buffers are HCO^{3-}, phosphate (HPO_4^{2-}), and ammonia (NH_3). Bicarbonate ions, which are present in the urine filtrate, combine with H^+ that has been secreted into the tubular fluid, resulting in formation of carbon dioxide and water. The carbon dioxide is then absorbed into the tubular cells and bicarbonate is regenerated. The phosphate ion is a metabolic end product that is filtered into the tubular fluid; it combines with a secreted hydrogen ion and is not reabsorbed. Ammonia is synthesized in tubular cells by deamination of the amino acid glutamine; it diffuses into the

tubular fluid and combines with the hydrogen ion. An important aspect of this buffer system is that the deamination process increases whenever the body's hydrogen ion concentration remains elevated for 1 to 2 days.

1.23 Elimination of Organic Ions

The proximal tubule actively secretes large amounts of different organic anions. Exogenous anions (e.g., salicylates, penicillin) and those produced endogenously (e.g., bile acids, uric acid) are actively secreted into the tubular fluid. Most of the anions that are secreted use the same transport system, allowing the kidneys to rid the body of many different drugs and environmental agents. Because the same transport system is shared by different anions, there is competition for transport such that elevated levels of one substance tend to inhibit the secretion of other anions. The proximal tubules also possess an active transport system for organic cations that is analogous to that for organic anions.

1.24 Uric Acid Elimination

Uric acid is a product of purine metabolism. Excessively high blood levels (i.e., hyperuricemia) can cause gout, and excessive urine levels can cause kidney stones. Uric acid is freely filtered in the glomerulus and is reabsorbed and secreted into the proximal tubules, using the previously described anion transport system in the proximal tubule. Tubular reabsorption normally exceeds secretion, and the net effect is removal of uric acid from the filtrate. Although the rate of reabsorption exceeds secretion, the secretory process is homeostatically controlled to maintain a constant plasma level. Many persons with elevated uric acid levels secrete less uric acid than do persons with normal uric acid levels. Uric acid uses the same

transport systems as other anions, such as aspirin, sulfinpyrazone, and probenecid. Small doses of aspirin compete with uric acid for secretion into the tubular fluid and reduce uric acid secretion, and large doses compete with uric acid for reabsorption and increase uric acid excretion in the urine. Because of its effect on uric acid secretion, aspirin is not recommended for treatment of gouty arthritis. Thiazide and loop diuretics (i.e., furosemide and ethacrynic acid) also can cause hyperuricemia and gouty arthritis, presumably through a decrease in extracellular fluid volume and enhanced uric acid reabsorption.

1.25 Urea Elimination

Urea is an end product of protein metabolism. The normal adult produces 25 to 30 g of urea a day; the quantity rises when a high-protein diet is consumed, when there is excessive tissue breakdown, or in the presence of gastrointestinal bleeding. With gastrointestinal bleeding, blood proteins are broken down to form ammonia in the intestine. The ammonia is then absorbed into the portal circulation and converted to urea by the liver before being released into the bloodstream. The kidneys, in their role as regulators of blood urea nitrogen (BUN) levels, filter urea in the glomeruli and then reabsorb it in the tubules. This enables maintenance of a normal BUN level, which ranges from 8 to 25 mg/dL (2.9 to 8.9 mmol/L). During periods of dehydration, the blood volume and GFR drop, and BUN levels increase. The renal tubules are permeable to urea, which means that the longer the tubular fluid remains in the kidneys, the greater is the reabsorption of urea into the blood. Only small amounts of urea are reabsorbed into the blood when the GFR is high, but relatively large amounts of urea are returned to the blood when the GFR is reduced.

1.26 Drug Elimination

Many drugs are eliminated in the urine. These drugs are selectively filtered in the glomerulus and reabsorbed or secreted into the tubular fluid. Drugs that are not bound to plasma proteins are filtered in the glomerulus and therefore able to be eliminated by the kidneys. Many drugs are weak acids or weak bases and are present in the renal tubular fluid partly as ionized water-soluble and nonionized lipid-soluble molecules. The nonionized lipid soluble form of a drug diffuses more readily across the lipid bilayer of the tubular cell membrane and then back into the bloodstream, whereas the ionized water-soluble form remains in the urine filtrate. The ratio of ionized to nonionized drug depends on the pH of the urine.

Aspirin, for example, is highly ionized in alkaline urine an in this form is rapidly excreted in the urine, and it is largely nonionized in acid urine and, as such, reabsorbed rather than excreted. Measures that alkalinize or acidify the urine may be used to increase elimination of drugs, particularly in situations of toxic overdose. Endocrine functions of the kidney in addition to their role in regulating fluid and electrolytes, the kidneys function as an endocrine organ in that they produce chemical mediators that travel through the blood to distant sites where they exert their actions. The kidneys participate in control of blood pressure through the renin-angiotensin-aldosterone mechanism, in calcium metabolism by activating vitamin D, and in regulating red blood cell production through the synthesis of erythropoietin (Port, 2011).

1.27 The Renin-Angiotensin-Aldosterone Mechanism

The renin-angiotensin-aldosterone mechanism is important in short- and long-term regulation of blood pressure. Renin is an enzyme that is synthesized and stored in the juxtaglomerular cells of

the kidney. This enzyme is thought to be released in response to a decrease in renal blood flow or a change in the composition of the distal tubular fluid, or as the result of sympathetic nervous system stimulation. Renin itself has no direct effect on blood pressure. Rather, it acts enzymatically to convert a circulating plasma protein called angiotensinogen to angiotensin I.

Angiotensin I, which has few vasoconstrictor properties, leaves the kidneys and enters the circulation; as it is circulated through the lungs, the angiotensin-converting enzyme catalyzes its conversion to angiotensin II. Angiotensin II is a potent vasoconstrictor, and it acts directly on the kidneys to decrease salt and water excretion. Both mechanisms have relatively short periods of action. Angiotensin II also stimulates the secretion of aldosterone by the adrenal gland, thereby exerting a more long-term effect on maintenance of blood pressure by increasing the reabsorption of sodium in the distal tubule. Renin also functions via angiotensin II to produce constriction of the efferent arteriole as a means of preventing a serious decrease in glomerular filtration pressure.

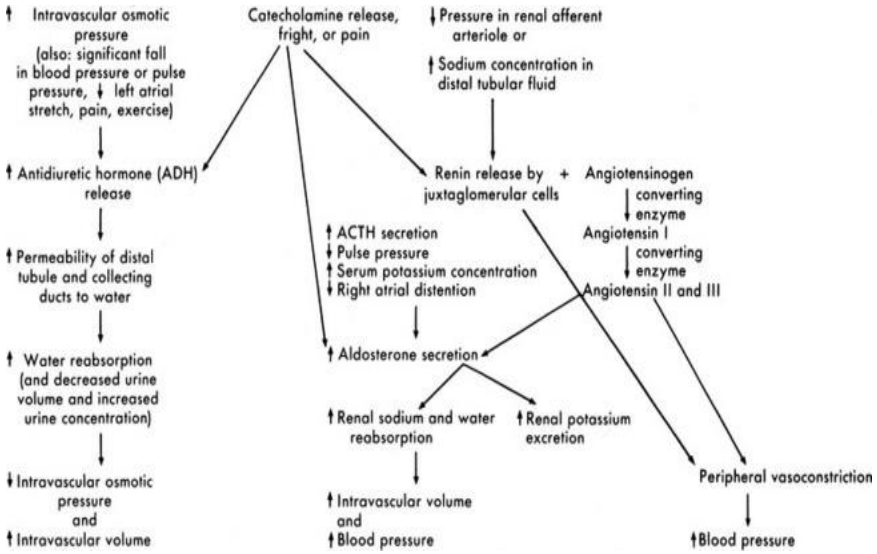


Figure 1.13 Renal response to changes in extracellular fluid volume and electrolyte concentration or stress

1.28 Renin, Aldosterone, and Antidiuretic Hormone

Renin is secreted from the polkissen cells of the afferent arteriole in the juxtaglomerular apparatus. In turn, renin forms angiotensin I from renin substrate (a circulating peptide from the liver). The amounts of renin released and angiotensin formed are determined by the renal perfusion pressure, sympathetic nervous system stimulation, circulating vasoactive substances, and changes in electrolyte concentration.

Angiotensin I circulates to the lung and is converted enzymatically to angiotensin II. Angiotensin II produces peripheral vasoconstriction and an increase in aldosterone secretion, which increases renal sodium and water reabsorption. These effects should increase intravascular volume. Angiotensin I and II are destroyed by angiotensinase, an enzyme that is present in plasma and secreted by a variety of organs, such as the kidney, intestine, and liver.

The quantity of sodium that is excreted in the urine when aldosterone is absent totals approximately 2% of the total filtered sodium. If aldosterone is absent (e.g., in patients with untreated adrenal insufficiency), excretion of that sodium will be associated with excretion of a large volume of water that can produce hypovolemic shock. Thus, aldosterone is responsible for the reabsorption of a very small but significant portion of the filtered sodium.

Aldosterone is secreted by the adrenal cortex in response to pituitary adrenal corticotropic hormone (ACTH) secretion and a variety of other stimuli. A fall in the pulse pressure, decreased stretch of the right atrium, and an increased serum potassium concentration all stimulate aldosterone secretion.63 An important stimulus for aldosterone is formation of angiotensin from renin released by the juxtaglomerular apparatus. Aldosterone stimulates epithelial cell transport of sodium in the renal tubular epithelium, along the intestinal lumen, and in sweat and saliva. Increased aldosterone levels increase the active reabsorption of sodium and decrease potassium reabsorption. The increased sodium reabsorption produces water reabsorption; this increases intravascular volume and reduces the juxtamedullary secretion of renin. The reduction in potassium tubular reabsorption increases potassium excretion in the urine and should result in a fall in the serum potassium concentration. These responses to aldosterone should in turn reduce the stimulus for aldosterone secretion.

Antidiuretic hormone (ADH), or arginine vasopressin (AVP), secretion also affects the final concentration of urine. ADH is produced by the supraoptic and paraventricular nuclei in the hypothalamus and is transported to the posterior lobe of the pituitary, where it is released in response to an increase in serum osmolality. ADH secretion is stimulated by serum osmolality greater than 280

to 285 mOsm/L (or a rise in serum osmolality of 2% or more). It also is secreted in response to significant (10%-15%) volume depletion, a fall in blood pressure, painful stimuli, fear, and exercise. Hemoconcentration, diabetic ketoacidosis,90 and mannitol administration increase ADH secretion, and administration of hypertonic glucose often inhibits ADH secretion. The predominant stimulus for ADH secretion is a rise in serum osmolality sensed by osmoreceptors in and around the supraoptic nucleus of the hypothalamus.

If ADH is present, the renal distal tubule and collecting ducts become highly permeable to water. As the collecting ducts descend through the hypertonic interstitium in the renal medulla, water will move from the collecting ducts into the medullary interstitium to be reabsorbed into the circulation. Thus, ADH secretion reduces urine volume and increases urine concentration.

If ADH levels are low, ADH secretion is absent (i.e., neurogenic diabetes inspidus [DI]), or the kidney is unresponsive to ADH (i.e., nephrogenic DI), the distal tubule and collecting ducts remain relatively impermeable to water, so water will remain in the filtrate that flows into the renal calyces. Large quantities of dilute urine will then be excreted.

1.29 Erythropoietin

Erythropoietin is a polypeptide hormone that regulates the differentiation of red blood cells in the bone marrow. Between 89% and 95% of erythropoietin is formed in the kidneys. The synthesis of erythropoietin is stimulated by tissue hypoxia, which may be brought about by anemia, residence at high altitudes, or impaired oxygenation of tissues due to cardiac or pulmonary disease. Persons with chronic kidney disease often are anemic because of an inability of the kidneys to produce erythropoietin. This anemia usually is

managed by the administration of a recombinant erythropoietin (epoetin alfa) produced through DNA technology to stimulate erythropoiesis.

1.30 Vitamin D

Activation of vitamin D occurs in the kidneys. Vitamin D increases calcium absorption from the gastrointestinal tract and helps to regulate calcium deposition in bone. It also has a weak stimulatory effect on renal calcium absorption. Although vitamin D is not synthesized and released from an endocrine gland, it is often considered as a hormone because of its pathway of molecular activation and mechanism of action.

Vitamin D exists in two forms: natural vitamin D (cholecalciferol), produced in the skin from ultraviolet irradiation, and synthetic vitamin D (ergocalciferol), derived from irradiation of ergosterol. The active form of vitamin D is 1,25-dihydroxycholecalciferol. Cholecalciferol and ergocalciferol must undergo chemical transformation to become active: first to 25-hydroxycholecalciferol in the liver and then to 1,25-dihydroxycholecalciferol in the kidneys. Persons with end-stage renal disease are unable to transform vitamin D to its active form and may require pharmacologic preparations of the active vitamin (calcitriol) for maintaining mineralization of their bones.

1.31 Tests of Renal Function

The function of the kidneys is to filter the blood, selectively reabsorb those substances that are needed to maintain the constancy of body fluid, and excrete metabolic wastes. Blood and urine tests can provide valuable information about the kidneys' ability to remove metabolic wastes and maintain the blood's normal

electrolyte and pH composition. As renal function declines, there is an increase in serum levels of substances such as urea, creatinine, phosphate, and potassium. Radiologic tests, endoscopy, and renal biopsy afford means for viewing the gross and microscopic structures of the kidneys and urinary system.

1.32 Renal Clearance and Glomerular Filtration Rate

Both the renal clearance and GFR provide information about the kidneys' ability to filter and reabsorb and/or secrete substances into blood. Renal clearance measures the rate at which a substance is excreted into the urine and the GFR measures the volume of plasma that is filtered each minute. In clinical practice, one way of estimating the clearance rate of endogenous creatinine is by collecting timed samples of blood and urine. Creatinine is a product of creatine metabolism in muscles; its formation and release are relatively constant and proportional to the amount of muscle mass present. Because creatinine is freely filtered in the glomeruli but is not reabsorbed from the tubules into the blood nor significantly secreted into the tubules from the blood, its blood and urine levels can be used to calculate the GFR. Another serum protein, cystatin C can also be used as an estimate of GFR. It is produced by all body cells at a constant rate, is freely filtered at the glomerulus, and in several studies has shown a greater sensitivity in detecting a decrease in GFR than creatinine. Recent studies suggest that the use of a combined creatinine–cystatin C equation may provide a better estimate of GFR than either test used separately.

1.33 Blood Tests

Blood tests can provide valuable information about the kidneys' ability to remove metabolic wastes from the blood and maintain normal electrolyte and pH composition of the blood. Serum levels of potassium, phosphate, BUN, and creatinine increase in renal failure while serum pH, calcium, and bicarbonate levels decrease.

1.34 Serum Creatinine

Serum creatinine levels reflect the GFR. Because these measurements are easily obtained and relatively inexpensive, they often are used as a screening measure of renal function. The normal creatinine value is approximately 0.7 mg/dL of blood for a woman with a small frame, approximately 1.0 mg/dL of blood for a normal adult man, and approximately 1.5 mg/dL of blood (60 to 130 mmol/L) for a muscular man. There is an age-related decline in creatinine clearance in many elderly persons because muscle mass and the GFR decline with age. A normal serum creatinine level usually indicates normal renal function. In addition to its use in calculating the GFR, the serum creatinine level is used in estimating the functional capacity of the kidneys. If the value doubles, the GFR—and renal function—probably has fallen to one half of its normal state. A rise in the serum creatinine level to three times its normal value suggests that there is a 75% loss of renal function, and with creatinine values of 10 mg/dL or more, it can be assumed that approximately 90% of renal function has been lost.

1.35 Blood Urea Nitrogen

Urea is formed in the liver as a by-product of protein metabolism and is eliminated entirely by the kidneys. Therefore, the BUN is related to the GFR but, unlike creatinine, it also is influenced by protein intake, gastrointestinal bleeding, and hydration status. In gastrointestinal bleeding, the blood is broken down by the intestinal flora, and the nitrogenous waste is absorbed into the portal vein and transported to the liver, where it is converted to urea. During dehydration, elevated BUN levels result from increased concentration. Approximately two thirds of renal function must be lost before a significant rise in the BUN level occurs. The BUN is less specific for renal insufficiency than creatinine, but the BUN–creatinine ratio may provide useful diagnostic information. The ratio normally is approximately 10:1. Ratios greater than 15:1 represent prerenal conditions, such as congestive heart failure and upper gastrointestinal tract bleeding, that produce an increase in BUN but not in creatinine. A ratio of less than 10:1 occurs in persons with liver disease and in those who receive a low-protein diet or chronic dialysis because BUN is more readily dialyzable than creatinine.

1.36 Urine Tests

Urine is a clear, amber-colored fluid that is approximately 95% water and 5% dissolved solids. The kidneys normally produce approximately 1.5 L of urine each day. Normal urine contains metabolic wastes and few or no plasma proteins, blood cells, or glucose molecules. Urine tests can be performed on a single urine specimen or on a 24-hour urine specimen. First-voided morning specimens are useful for qualitative protein and specific gravity testing. A freshly voided specimen is most reliable. Urine specimens that have been left standing may contain lysed red blood cells,

disintegrating casts, and rapidly multiplying bacteria. Casts are molds of the distal nephron lumen. A gel like substance called Tamm-Horsfall mucoprotein, which is formed in the tubular epithelium, is the major protein constituent of urinary casts. Casts composed of this gel but devoid of cells are called hyaline casts. These casts develop when the protein concentration of the urine is high (as in nephrotic syndrome), urine osmolality is high, and urine pH is low. The inclusion of granules or cells in the matrix of the protein gel leads to the formation of various other types of casts.

1.37 Proteinuria

Proteinuria represents excessive protein excretion in the urine. Because of the glomerular capillary filtration barrier, less than 150 mg/L of protein is excreted in the urine over 24 hours in a healthy person. Urine tests for proteinuria are used to detect abnormal filtering of albumin in the glomeruli or defects in its reabsorption in the renal tubules. A protein reagent dipstick can be used as a rapid screening test for the presence of proteins in the urine. Once the presence of proteinuria has been detected, a 24-hour urine test is often used to quantify the amount of protein that is present. Albumin, which is the smallest of the plasma proteins, is filtered more readily than globulins or other plasma proteins. Thus, microalbuminuria tends to occur long before clinical proteinuria becomes evident. A dipstick test for microalbuminuria is available for screening purposes. The microalbuminuria dipstick method, however, only indicates an increase in urinary albumin that is below the detectable range of the standard proteinuria test. It does not specify the amount of albumin that is present in the urine. Therefore, a 24-hour urine collection is the standard method for detecting microalbuminuria (an albumin excretion >30 mg/day is abnormal).

1.38 Specific Gravity and Osmolality

The specific gravity of urine is a measure of its concentration of solutes. Urine specific gravity provides a valuable index of the hydration status and functional ability of the kidneys. The usual range is from 1.010 to 1.025 with normal fluid intake. Healthy kidneys can produce concentrated urine with a specific gravity of 1.030 to 1.040 during periods of dehydration, and a dilute urine with a specific gravity that approaches 1.000 during periods of taking too much fluid. With diminished renal function, there is a loss of renal concentrating ability, and the urine specific gravity may fall to levels of 1.006 to 1.010. These low levels are particularly significant if they occur during periods that follow a decrease in water intake (e.g., during the first urine specimen on arising in the morning).Urine osmolality, which depends on the number of particles of solute in a unit of solution, is a more exact measurement of urine concentration than specific gravity. More information concerning renal function can be obtained if the serum and urine osmolality tests are done at the same time. The normal ratio between urine and serum osmolality is 3:1. A high urine-to-serum ratio is seen in concentrated urine. With poor concentrating ability, the ratio is low.

CHAPTER 2

ACUTE KIDNEY INJURY

2.1 Classification of Kidney Dysfunction

Kidney injury may be acute and rapidly progressive (within hours), and the process may be reversible. Kidney failure also can be chronic, progressing to end-stage kidney failure over a period of months or years. The terms *renal insufficiency*, *renal failure*, *uremia,* and *azotemia* are associated with decreasing renal function but are not specific in relation to cause of kidney disease. Often they are used synonymously, although with some distinctions. Generally, **renal insufficiency** refers to a decline in renal function to about 25% of normal or a GFR of 25 to 30 ml/minute. Levels of serum creatinine and urea are mildly elevated.

Renal failure refers to significant loss of renal function. When less than 10% of renal function remains, this is termed **end-stage kidney disease (ESKD).** Specific criteria for acute renal dysfunction are discussed in the next section. **Uremia** is a syndrome of renal failure and includes elevated blood urea and creatinine levels accompanied by fatigue, anorexia, nausea, vomiting, pruritus, and neurologic changes. Uremia represents numerous consequences related to renal failure, including retention of toxic wastes, deficiency states, electrolyte disorders, and immune activation promoting a proinflammatory state. **Azotemia** is characterized by

increased serum urea levels and frequently increased creatinine levels as well. Renal insufficiency or renal failure causes azotemia. Both azotemia and uremia indicate an accumulation of nitrogenous waste products in the blood, a common characteristic that explains the overlap in definitions of terms.

Table 2.1 RIFLE Criteria for acute renal dysfunction/failure

Category	GFR criteria	Urine Output (UO) criteria
Risk	Increased creatinine × 1.5 or GFR decrease > 25 %	UO <0.5 ml/kg/h for 6 h
Injury	Increased creatinine × 2 or GFR decrease > 50 %	UO <0.5 ml/kg/h for 12 h
Failure	Increase creatinine × 3 or GFR decrease > 75 %	UO <0.3 ml/kg/h for 24 h or anuria for 12 h
Loss	Persistent ARF = complete loss of kidney function >4 wk	
ESKD	End-stage kidney disease (>3 mo)	

2.2 Acute Kidney Injury

Acute kidney injury (AKI) affects about 5% of hospitalized individuals and has a mortality of 50% to 80%. AKI is a sudden decline in kidney function with a decrease in glomerular filtration and accumulation of nitrogenous waste products in the blood as demonstrated by an elevation in plasma creatinine and blood urea nitrogen levels. The term acute kidney injury is preferred to the term acute renal failure because it captures the diverse nature of this syndrome, ranging from minimal or subtle changes in renal function to complete renal failure requiring renal replacement therapy. classification criteria have been developed to guide the diagnosis of renal injury described by the acronym RIFLE (R = risk, I = injury, F = failure, L = loss, and E = end-stage kidney disease [ESKD])

representing renal dysfunction of increasing severity (Bellomo et al., 2004)(Cruz et al., 2010).

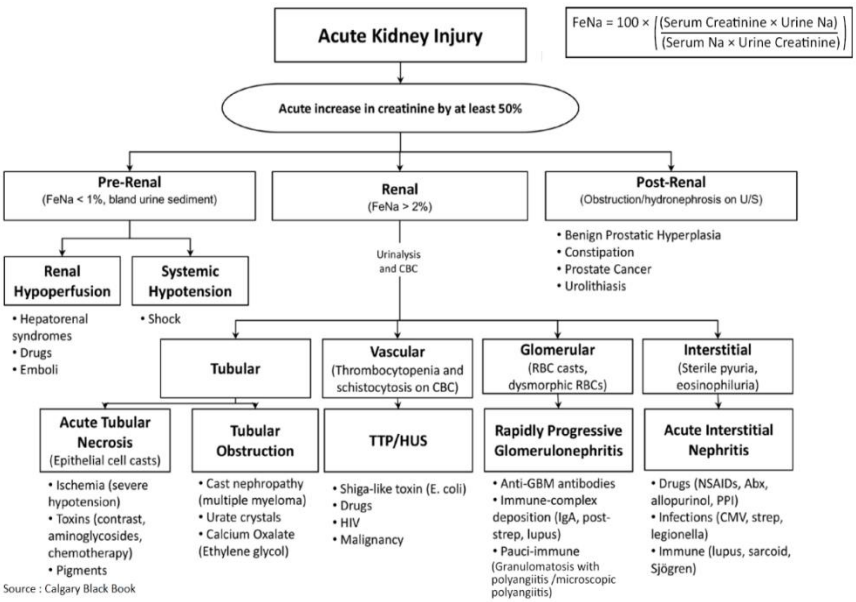


Figure 2.1 Pathway acute kidney injury

2.3 Pathophysiology

AKI commonly results from extracellular volume depletion, decreased renal blood flow, or oxic/inflammatory injury to kidney cells that results in alterations in renal function that may be minimal or severe. Even small changes in renal function may be associated with significant morbidity and mortality. The etiologies of AKI can be described considering three categories of injury: (1) renal hypoperfusion (prerenal AKI); (2) disorders involving the renal parenchymal or interstitial tissue (intrarenal or intrinsic AKI); and (3) disorders associated with acute urinary tract obstruction (postrenal AKI). Most types of AKI are reversible if diagnosed and treated early.

Comparing types of AKI

Depending on the cause, acute kidney injury (AKI) can be prerenal, intrinsic, or postrenal. The table below describes each type and its causes.

Type of kidney injury	Causes
Prerenal injury: decreased renal blood flow resulting from sepsis, trauma, bleeding, or poor cardiac output	• Prolonged low-volume states, such as sepsis, decreased blood pressure, and hemorrhage • Such drugs as nonsteroidal anti-inflammatory agents or cyclooxygenase inhibitors, which inhibit prostaglandin synthesis; in turn, inhibition triggers action of vasoconstrictors on renal arterioles, which decreases glomerular filtration rate.
Intrinsic injury: acute tubular necrosis from sepsis and renal ischemia (mean arterial pressure below 70 mm Hg) and ultimately, from poor organ perfusion and multisystemic failure	• Nephropathy caused by contrast agents • Aminoglycoside drug therapy without careful dosage monitoring
Postrenal: obstructive nephropathy resulting from mechanical obstruction of urine flow	• Renal calculi • Tumors • Prostatic hypertrophy • Strictures • Congenital defects

Table 2.2 Types of AKI

2.4 Prerenal Acute Kidney Injury

Prerenal acute kidney injury is the most common cause of AKI. Reduced effective arterial blood volume causes renal hypoperfusion that occurs rapidly over a period of hours with elevation of BUN and plasma creatinine levels. During the early phases of hypoperfusion protective autoregulatory mechanisms maintain GFR at a relatively constant level through afferent arteriolar dilation and efferent arteriolar vasoconstriction (mediated by angiotensin II). tubuloglomerular feedback mechanisms also maintain GFR and distal tubular nephron flow. The GFR ultimately declines because of the decrease in filtration pressure. Poor perfusion can result from renal artery thromobosis, hypotension related to hypovolemia (dehydration, diarrhea, fluid shifts) or hemorrhage, renal vasoconstriction and alterations in renal regional blood flow,

microthrombi, or kidney edema that restricts arterial blood flow (Bouglé & Duranteau, 2011).

Sepsis/septic shock and cardiogenic shock following cardiac surgery are the most common causes of AKI in the intensive care unit (Bellomo et al., 2012). AKI may occur during chronic kidney failure if a sudden stress is imposed on already marginally functioning kidneys, hastening the progression to end-stage kidney disease. Failure to restore blood volume or blood pressure and oxygen delivery can cause cell injury and acute tubular necrosis and apoptosis or acute interstitial necrosis, a more severe form of AKI.

2.5 Intrarenal (intrinsic) Acute Kidney Injury

Intrarenal (intrinsic) acute kidney injury (AKI) may result from ischemic acute tubular necrosis (ATN), nephrotoxic ATN (i.e., exposure to radiocontrast media or antibiotics), acute glomerulonephritis, vascular disease (malignant hypertension, disseminated intravascular coagulation, and renal vasculitis), allograft rejection, or interstitial disease (drug allergy, infection, tumor growth). Acute tubular necrosis (ATN) caused by ischemia is the most common cause of intrarenal AKI. It occurs most often after surgery (40% to 50% of cases) but is also associated with severe sepsis; obstetric complications; and severe trauma, including severe burns; or small vessel vasculitis. A combination of events and predisposing factors leads to the greatest risk for acute renal failure.

The terms acute tubular necrosis and acute kidney injury are sometimes used interchangeably, but the conditions are not the same because acute kidney injury can occur without ATN. ATN is generally described as postischemic or nephrotoxic or it can be a combination of both. Postischemic ATN involves persistent hypotension, hypoperfusion, and hypoxemia, producing ischemia and reduced levels of ATP and generating toxic oxygen-free radicals

with loss of antioxidant protection that causes cell swelling, injury, and necrosis. Activation of inflammatory cells (e.g., neutrophils, macrophages, and lymphocytes) and complement and release of inflammatory cytokines contribute to tubular injury (Lee et al., 2011). Transport of sodium and other molecules is disrupted with damage primarily to the proximal tubular epithelium and shedding of the brush border with the appearance of tubular granular casts in the urine. Ischemic necrosis tends to be patchy and may be distributed along any part of the nephron tubules. Injury is most severe in the outer medulla with scattered necrosis in the cortex and loss of cells along the tubular epithelium (Bonventre & Yang, 2011).

Severe disease of the glomeruli (i.e., acute or rapidly progressive glomerulonephritis) or renal microvascular disorders can also cause intrinsic kidney injury. Oliguria is common (urine output less than 30 ml/hour) with intrarenal AKI, but anuria is rare. Creatinine values in septic renal injury may not reflect renal injury because sepsis decreases production of creatinine without major alterations in body weight, hematocrit level, or amount of extracellular fluid. Creatinine level usually increases with decreased renal blood flow and decreased GFR. However, in sepsis-induced AKI, creatinine values can remain within normal ranges and may be related to alterations in intrarenal microcirculatory blood flow that are different from the kidney ischemia that develops related to systemic hypotension and hypoperfusion of nonseptic AKI (Honore et al., 2011) (Zarjou & Agarwal, 2011).

Nephrotoxic ATN can be produced by numerous antibiotics, but the aminoglycosides (gentamicin, tobramycin) are the major culprits. The drugs tend to accumulate in the renal cortex and may not cause renal failure until after treatment is complete. Radiocontrast media (x-ray media) and cisplatin also may be nephrotoxic. Dehydration, advanced age, concurrent renal

insufficiency, and diabetes mellitus tend to enhance nephrotoxicity from either aminoglycosides or radiocontrast media. Other substances such as carbon tetrachloride, heavy metals (mercury, arsenic), methoxyflurane anesthesia, or bacterial toxins may promote renal failure. Endogenous substances toxic to renal tubules are excessive myoglobin (oxygen-transporting substance in muscles) and hemoglobin. Necrosis and tubular cell apoptosis caused by nephrotoxins are usually uniform and limited to the proximal tubules. The high surface area of the brush border (microvilli) of the proximal tubular cells and the reabsorption properties of epithelial cells make them more vulnerable to toxic injury (Ortiz et al., 2003).

2.6 Postrenal Acute Kidney Injury

Postrenal acute kidney injury is rare and usually occurs with urinary tract obstruction that affects the kidneys bilaterally (e.g., bilateral ureteral obstruction, bladder outlet obstruction–prostatic hypertrophy, tumors or neurogenic bladder, and urethral obstruction). The obstruction causes an increase in intraluminal pressure upstream from the site of obstruction with a gradual decrease in GFR. A pattern of several hours of anuria with flank pain followed by polyuria is a characteristic finding. This type of AKI can occur after diagnostic catheterization of the ureters, a procedure that may cause edema with obstruction of the tubular lumen.

2.7 Oliguria

Oliguria (less than 400 ml of urine output per day) can occur in AKI, and three mechanisms have been proposed to account for the decrease in urine output. All three mechanisms probably contribute to oliguria in varying combinations and degrees throughout the

course of the disease. These mechanisms are as follows (Clarkson et al., 2007):

1. Alterations in renal blood flow. Efferent arteriolar vasoconstriction may be produced by intrarenal release of angiotensin II or by redistribution of blood flow from the cortex to the medulla. Autoregulation of blood flow may be impaired, resulting in decreased GFR. Changes in glomerular permeability and decreased GFR also may result from the ischemia.
2. Tubular obstruction. Advanced injury with necrosis of the tubules causes sloughing of cells, cast formation, or ischemic edema that results in tubular obstruction, which in turn causes a retrograde increase in pressure and reduces the GFR. Renal failure can occur within 24 hours.
3. Backleak. Glomerular filtration remains normal, but tubular reabsorption or “leak” of filtrate is accelerated as a result of permeability caused by ischemia and increased tubular pressure from obstruction.

Table 2.3 Four phases of AKI

Four phases of AKI		
This chart describes the features and durations of the four phases of acute kidney Injury (AKI).		
Phase	**Features**	**Duration**
Onset phase	• Common triggering events: significant blood loss, bums. fluid loss, diabetes Insipidus • Renal blood flow of normal • Tissue oxygenation 25% of normal • Urine output below 0.5 mL/kg/hour	Hours to days
Oliguric (anuric) phase	• Urine output below 400 mL/day, possibly as low as 100 mL/day • Increases In blood urea nitrogen (BUN) and creatinine levels • Electrolyte disturbances. acidosis, and fluid overload (from kidneys Inability to excrete water)	8 to 14 days or longer, depending on nature of AKI and dialysis Initiation
Diuretic phase	• Occurs when cause of AKI Is corrected • Renal tubule scarring and edema • Increased glomerular filtration rate (GER) • Daily urine output above 400 mL • Possible electrolyte depletion from excretion of more water and osmotic effects of BUN	7 to 14 days
Recovery phase	• Decreased edema • Normalization of fluid and electrolyte balance • Return of of normal	Several months to 1 year

2.8 Clinical Manifestations.

The clinical progression of acute kidney injury, particularly acute tubular necrosis, occurs in three phases: initiation phase, maintenance phase, and recovery phase. The initiation phase is the phase of reduced perfusion or toxicity in which renal injury is evolving, usually lasting 24 to 36 hours. Prevention of injury is possible during thisphase. The maintenance or oliguric phase is the period of established renal injury and dysfunction after the initiating event has been resolved and may last from weeks to months. Urine output is lowest during this phase, and serum creatinine, blood urea nitrogen, and serum potassium levels increase; metabolic acidosis

develops; and there is salt and water overload. The recovery phase is the interval when renal injury is repaired and normal renal function is reestablished. GFR returns toward normal but the regenerating tubules cannot concentrate the filtrate. Diuresis is common during this phase, with a decline in serum creatinine and urea levels and an increase in creatinine clearance. Polyuria can result in excessive loss of sodium, potassium, and water. Fluid and electrolyte balance requires careful maintenance.

Table 2.4 Classification and differential diagnosis of AKI

Classification and differential diagnosis of acute kidney injury.

			Intrinsic Renal Disease		
	Prerenal Azotemia	Postrenal Azotemia	Acute Tubular Necrosis (Oliguric or Polyuric)	Acute Glomerulonephritis	Acute Interstitial Nephritis
Etiology	Poor renal perfusion	Obstruction of the urinary tract	Ischemia, nephrotoxins	Immune complex-mediated, pauci-immune, anti-GBM related	Allergic reaction; drug reaction; infection, collagen vascular disease
Serum BUN:Cr ratio	> 20:1	> 20:1	< 20:1	> 20:1	< 20:1
Urinary indices					
U_{Na} (mEq/L)	< 20	Variable	> 20	< 20	Variable
FE_{Na} (%)	< 1	Variable	> 1 (when oliguric)	< 1	< 1; > 1
Urine osmolality (mOsm/kg)	> 500	< 400	250–300	Variable	Variable
Urinary sediment	Benign or hyaline casts	Normal or red cells, white cells, or crystals	Granular (muddy brown) casts, renal tubular casts	Red cells, dysmorphic red cells and red cell casts	White cells, white cell casts, with or without eosinophils

BUN:Cr, blood urea nitrogen:creatinine ratio; Fe_{Na}, fractional excretion of sodium; GBM, glomerular basement membrane; U_{Na}, urinary concentration of sodium. Source : Current Medical Diagnosis and Treatment

Oliguria begins within 1 day after a hypotensive event and lasts for 1 to 3 weeks, but it may regress in several hours or extend for several weeks, depending on the duration of ischemia or severity of toxic injury and the initiation of treatment. Anuria (urine output less than 50 ml/day) is uncommon in ATN, and 10% to 20% of cases have nonoliguric failure. Anuria involves both kidneys and suggests

bilateral renal artery occlusion, obstructive uropathy, or acute cortical necrosis. Nonoliguric renal failure usually represents less severe injury and is associated with toxin exposure or drug toxicity.

The renal tubules have impaired reabsorption and concentration and dilution function. The urine output may be greater than 2 L per day, but the BUN and plasma creatinine concentrations increase. Other early manifestations depend on the underlying cause of renal failure. Individuals who have experienced trauma or surgery or people in a catabolic state may have more rapid elevations in BUN level. They are prone to hyperkalemia and metabolic acidosis related to decreased potassium level and hydrogen excretion. Renal phosphate excretion is decreased, causing hyperphosphatemia. Fluid retention may cause edema. Symptoms of congestive heart failure develop in persons with cardiac disease. Nausea, vomiting, and fatigue accompany uremia and electrolyte imbalances. Wound healing is delayed, and the risk of infection, particularly pneumonia, is greater.

Nonoliguric renal failure generally has a better prognosis because of fewer complications and regeneration of the tubular epithelium. Individuals with oliguria may require maintenance dialysis to attenuate symptoms of renal failure. As renal function improves during the recovery phase, increase in urine volume (diuresis) is progressive. During the early diuretic phase the tubules are still recovering secretory and reabsorptive function. Sodium and potassium are lost in the urine, and the risk for hypokalemia is greater. Volume depletion may ensue, with fluid losses of 3 to 4 L/day. Fluid and electrolyte balance must be carefully monitored and excessive urinary losses replaced. Return to normal status may take 3 to 12 months. Approximately 30% of individuals do not have full recovery of a normal GFR or tubular function and progress to end-stage kidney disease (Coca et al., 2012).

2.9 Evaluation and Treatment

Evaluation and treatment the diagnosis of AKI is related to the cause of the disease. The history can help distinguish the different etiologies of AKI. Prerenal causes are associated with a history of blood volume depletion or other causes of poor kidney perfusion (e.g., shock, heart failure, renal artery thrombi). Intrinsic causes include exposure to nephrotoxins and infection. Postrenal causes are associated with obstructive uropathies (e.g., an enlarged prostate or stones). The diagnostic challenge is to differentiate prerenal acute renal injury from acute tubular necrosis. Urine composition may provide helpful diagnostic clues to changes in tubular function.

The ratios of the BUN to plasma creatinine concentration and fractional excretion of sodium (the ratio of filtered sodium to excreted sodium) are helpful diagnostic indicators because the tests reflect renal tubular reabsorption ability. In prerenal AKI, tubular function is maintained and salt, water, and urea are reabsorbed. With ATN, reabsorption and urinary concentration abilities are compromised. Other causes of renal failure also may exhibit similar clinical findings. Cystatin C, a serum protein constantly produced by nucleated cells, is freely filtered by the glomerulus, and its concentration can serve as a measure of GFR and may be useful for detecting early changes in glomerular filtration rate (Odutayo & Cherney, 2012). Serial measurements of plasma creatinine concentration provide an index of renal function during the recovery phase. However, changes in serum creatinine level occur only if more than 50% of glomerular filtration is lost and are often delayed by more than 24 hours. Such diagnostic delays make the implementation of early therapy very difficult, contributing to disease progression and mortality. Advances are being made in the use of biomarkers that allow assessment of kidney injury before elevation of serum creatinine level.

Prevention of AKI and maintenance of renal perfusion involve maintenance of fluid volume before and after surgery or diagnostic procedures or when nephrotoxic drugs or contrast agents are in use. There is no specific treatment for acute renal failure. The primary goal of therapy, once AKI has occurred, is to maintain the individual's life until renal function has recovered. Management principles directly related to physiologic alterations generally include (1) correcting fluid and electrolyte disturbances, (2) managing blood pressure, (3) preventing and treating infections, (4) maintaining nutrition, and (5) remembering that certain drugs or their metabolites are not excreted and can be toxic. Fluid and electrolyte replacement must be carefully calculated with consideration of urine losses, insensible losses (up to 1000 ml/day), and production of endogenous water by oxidation (450 ml/day). Overhydration of patients dilutes their plasma sodium concentration.

Metabolic acidosis is usually not treated until serum bicarbonate concentration is less than 15 mEq/L (Sharfuddin et al., 2012). Hyperkalemia can be managed by restricting dietary sources of potassium, using non–potassium-sparing diuretics, or using cation ion exchange resins, which may be administered orally or rectally. These resins exchange potassium for another cation, such as sodium in the bowel, and the potassium is then excreted attached to the resin. With severe hyperkalemia (more than 6.5 mEq/L), dialysis may be required or potassium can be driven back temporarily into the cells by administering glucose and insulin or by infusing sodium bicarbonate or albuterol. Glucose metabolism causes potassium to move to the intracellular fluid, and insulin infusions therefore can be effective in shifting potassium from the extracellular to intracellular space, along with the transport of glucose, within 30 minutes. Using sodium bicarbonate to cause alkalemia also shifts potassium into

cells in exchange for hydrogen ions. However, use of sodium bicarbonate in AKI is controversial (Hewitt et al., 2012).

Careful monitoring of the electrocardiogram for peaking T waves is essential for individuals with hyperkalemia. Intravenous infusion of calcium is the most rapid method of treating cardiac effects of hyperkalemia. Calcium decreases the threshold potential and reduces the membrane excitability caused by hyperkalemia. Calcium should be used only in emergencies, however, because hypercalcemia also may cause cardiac arrest. Azotemia is generally controlled and nutrition maintained with a low-protein, high-carbohydrate diet. Essential amino acid replacement can be given orally or parenterally. Adequate carbohydrate intake slows protein catabolism and helps prevent release of potassium from cellular breakdown. Because sepsis is a common serious and potentially fatal complication of renal failure, observation for signs of infection and early treatment with antibiotics are necessary.

Drug dosage levels may require adjustment if they are metabolized or excreted by the kidneys. Recovery may take up to 1 year. Continuous renal replacement therapy (CRRT [hemodialysis]) (mechanical removal of water, electrolytes, and toxins from the blood) is indicated for uncontrollable hyperkalemia or acidosis or severe fluid overload. CRRT is particularly promising in critically ill people with multiple organ dysfunction or sepsis. The timing and optimal dose-response relationships for CRRT are under investigation (Joannidis & Forni, 2011) (Palevsky, 2013).

CHAPTER 3

CHRONIC KIDNEY DISEASE

Chronic kidney disease (CKD) is the progressive loss of renal function associated with systemic diseases such as hypertension, diabetes mellitus, systemic lupus erythematosus, or intrinsic kidney disease, including kidney stones, acute kidney injury, chronic glomerulonephritis, chronic pyelonephritis, obstructive uropathies, or vascular disorders. The National Kidney Foundation (www.kidney.org/professionals/) defines kidney damage as a GFR less than 60 ml/min/1.73 m2 for 3 months or more, irrespective of cause. *Chronic kidney disease* is the preferred terminology and is referenced to declining GFR. The terms *renal insufficiency* and *chronic renal failure* are still often used to describe declining renal function, but they do not have the specificity of the stages recommended by the National Kidney Foundation. CKD decreases filtration and tubular functions with consequences manifested throughout all organ systems.

Table 3.1 GFR

Stages	Description	GFR (mL/min/1.73 m²)
1	Kidney damage with normal or ↑ GFR	≥90
2	Kidney damage with normal or mild GFR ↓	60-89
3	Mild GFR ↓	30-59
4	Severe GRF ↓	15-29
5	Renal failure	<15 or dialysis

Chronic kidney disease is defined as the presence of kidney damage and/or GFR <60mL/minutes/1.73 m² for ≥3 months. Kidney damage is defined as pathologic abnormalities or damage markers, including abnormalities in blood or urine tests or radiological examinations.

3.1 Pathophysiology

The kidneys have a remarkable ability to adapt to loss of nephron mass. Symptomatic changes resulting from increased levels of creatinine, urea, and potassium and alterations in salt and water balance usually do not become apparent until renal function declines to less than 25% of normal when adaptive renal reserves have been exhausted. Different theories have been proposed to account for the adaptation to loss of renal function. The *intact nephron hypothesis* proposes that loss of nephron mass with progressive kidney damage causes the surviving nephrons to sustain normal kidney function. These nephrons are capable of a compensatory hypertrophy and expansion or hyperfunction in their rates of filtration, reabsorption, and secretion and can maintain adaptive changes in solute and water regulation in the presence of overall declining GFR.

Although the urine of an individual with chronic kidney failure may contain abnormal amounts of protein and red and white blood

cells or casts, the major end products of excretion are similar to those of normally functioning kidneys until the advanced stages of renal failure when there is a significant reduction of functioning nephrons (Yang et al., 2011). With severe or repeated injury, epithelial cells have an impaired proliferative response resulting in interstitial capillary loss and fibroblast proliferation. The progressive process of glomerulosclerosis and tubulointerstitial fibrosis contributes to end-stage kidney disease (Grgic et al., 2012). The *particular location of kidney damage* also can influence loss of kidney function. For example, tubular interstitial diseases damage primarily the tubular or medullary parts of the nephron, producing problems such as renal tubular acidosis, salt wasting, and difficulty diluting or concentrating the urine.

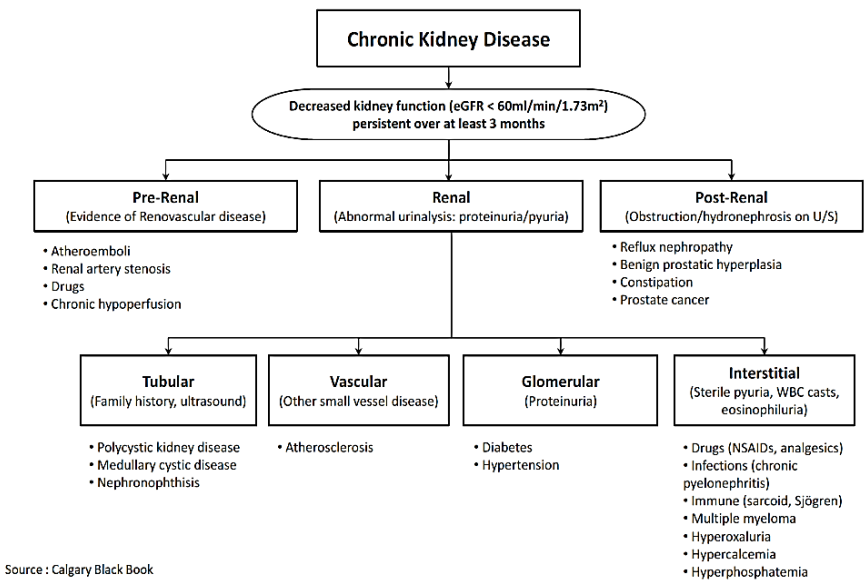


Figure 3.1 Chronic kidney disease pre, intra, post renal

When the damage is primarily vascular or glomerular, proteinuria, hematuria, and nephrotic syndrome are more prominent. The factors that contribute to the pathogenesis of CKD are complex and involve the interaction of many cells, cytokines, and structural alterations. Two factors that have consistently been recognized to advance renal disease are proteinuria and angiotensin II activity. Glomerular hyperfiltration and increased glomerular capillary permeability lead to proteinuria. Proteinuria contributes to tubulointerstitial injury by accumulating in the interstitial space and activating complement proteins and other mediators and cells, such as macrophages, that promote inflammation and progressive fibrosis (Gorriz & Martinez-Castelao, 2012).

Angiotensin II activity is elevated with progressive nephron injury. **Angiotensin II** promotes glomerular hypertension and hyperfiltration caused by efferent arteriolar vasoconstriction and also promotes systemic hypertension. The chronically high intraglomerular pressure increases glomerular capillary permeability, contributing to proteinuria. Angiotensin II also may promote the activity of inflammatory cells and growth factors that participate in tubulointerstitial fibrosis and scarring (Rüster & Wolf, 2011).

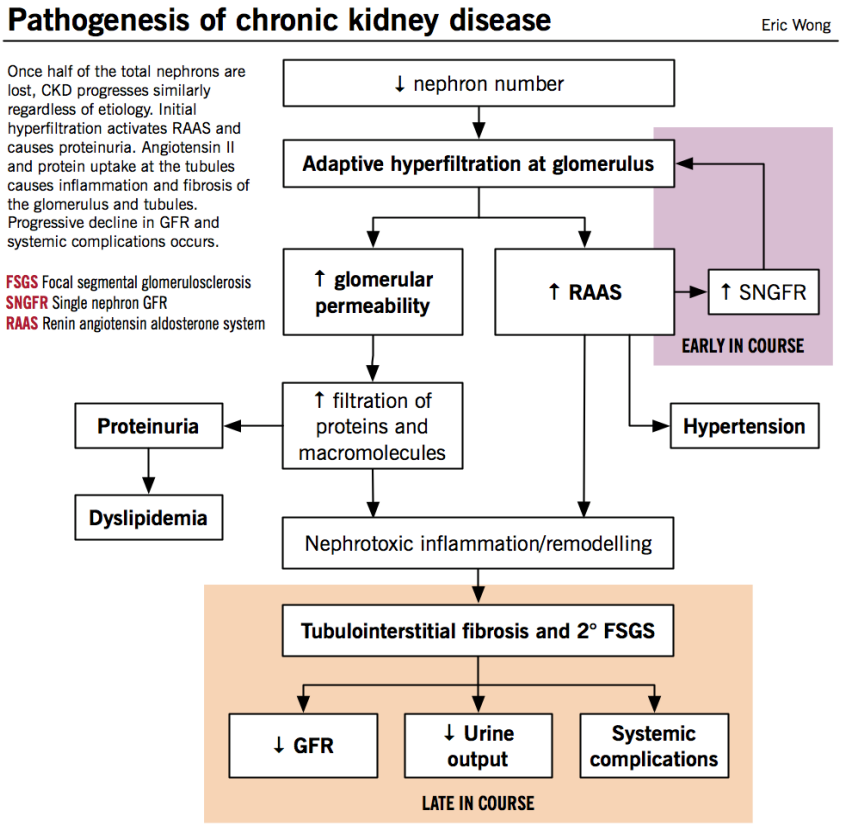


Figure 3.2 Pathogenesis of chronic kidney disease

3.2 Clinical Manifestations

The clinical manifestations of chronic kidney disease are often described using the terms azotemia and uremia. Azotemia is manifested by increased levels of serum urea, serum creatinine, and other nitrogenous compounds related to decreasing kidney function. Uremia is a pro inflammatory state with many systemic effects known as **uremic syndrome** (Libetta et al., 2011) and is associated with the accumulation of urea and other nitrogenous compounds and toxins. Sources of toxins include the accumulation of end products

of protein metabolism, alterations in fluid and electrolytes, metabolic acidosis, intestinal absorption of toxins produced by gut bacteria, and results of altered renal hormone synthesis (i.e., anemia, hyperphosphatemia, and hypocalcemia). Generally, the symptoms include hypertension, anorexia, nausea, vomiting, diarrhea or constipation, malnutrition and weight loss, pruritus, edema, anemia, and neurologic, cardiovascular disease, and skeletal changes.

3.3 Creatinine and Urea Clearance

Creatinine is constantly released from muscle and excreted primarily by glomerular filtration. In CKD, as the GFR declines, the plasma creatinine level increases by a reciprocal amount to maintain a constant rate of excretion. Because no significant tubular adjustment occurs for creatinine (i.e., tubular secretion), the plasma levels continue to increase as the GFR decreases. Therefore, measures of plasma creatinine can serve as an index of changing glomerular function. The clearance of *urea* follows a similar pattern, but urea is filtered as well as reabsorbed and varies with the state of hydration; it is not a good index of GFR. However, as the GFR decreases, plasma urea concentration also increases (Ferguson & Waikar, 2012).

3.4 Fluid and Electrolyte Balance

Fluid and electrolyte and acid-base balances are significantly disturbed with chronic kidney disease. Levels of *sodium* must be regulated within narrow limits because sodium is the major extracellular solute. In CKD sodium and water balance is maintained very close to normal until the development of stage V ESKD. This occurs because of the increased fractional excretion of sodium, particularly in the distal nephron, in relation to decreasing GFR.

Hormones including aldosterone, prostaglandins, and natriuretic peptides also modulate sodium excretion and their levels are elevated with progressive renal failure.

Individual variation in the underlying pathology of CKD must be considered in the management of sodium intake or restriction. Sodium wasting may be present with tubulointerstitial causes of CKD and there may also be extra renal losses of sodium from vomiting, diarrhea, or fever. Sodium retention is more likely in ESKD particularly in the presence of nephrotic syndrome or heart failure. Sodium retention contributes to hypertension, edema, heart failure, and mortality.

Management of salt and water balance requires individual assessment, and both hyponatremia and hypernatremia require management (Kovesdy, 2012). The regulation of *water balance* and osmolality is normally achieved by urinary concentration mediated by antidiuretic hormone (ADH). As GFR is reduced, ability to concentrate and dilute the urine diminishes. In earlier stages of renal failure, this may be caused by osmotic diuresis produced by increased fractional excretion of solutes by the remaining nephrons or by a decreased tubular response to ADH. Individual nephrons can maintain water balance until severe renal failure occurs and GFR declines to 15% to 20% of normal with extensive loss of nephron and tubular function. At this stage the urinary concentration becomes fixed and approaches that of the plasma at 285 mOsm/L with a specific gravity of about 1.010. Urinary excretion of *potassium* is related primarily to distal tubular secretion mediated by aldosterone and sodiumpotassium adenosine triphosphatase.

In renal failure there is increased tubular secretion that provides effective regulation until the onset of oliguria. With hyperkalemia larger amounts of potassium can be eliminated through the bowel (Sorensen et al., 2010). Although nonoliguric

patients can maintain potassium excretion with normal dietary intake, they are more prone to develop hyperkalemia with increased loading (i.e., use of salt substitutes). Use of potassium-sparing diuretics, such as spironolactone (aldactone), volume depletion, acute infection, severe acidosis, or marked hyperglycemia also may precipitate elevated levels of serum potassium (Lehnhardt & Kemper, 2011). With progression of disease to end-stage renal failure (ESRF), total body potassium can increase to life threatening levels and must be controlled by dietary restriction, loop diuretics, cation exchange resins, and dialysis.

Severe acute hyperkalemia is treated with intravenous calcium gluconate, intravenous dextrose and insulin, and nebulized or intravenous salbutamol (sympathetic beta2 agonist, promotes Na+-K+- ATPase pump and intracellular movement of potassium). Renal replacement therapy may be required (support of renal function using hemodialysis or peritoneal dialysis) (Fleming, 2011). The intake of a normal diet produces 50 to 100 mEq of hydrogen per day. These ions are secreted from the renal tubules and excreted in the urine combined with phosphate and ammonia buffers. *Metabolic acidosis* develops when GFR decreases to less than 20% to 25% of normal. The causes of acidosis are primarily related to decreased hydrogen ion elimination and decreased bicarbonate reabsorption. With end-stage renal failure, metabolic acidosis may be severe enough to require alkali therapy and dialysis. Bicarbonate levels should be maintained at about 22 mEq/L (Kraut & Madias, 2011).

3.5 Calcium, Phosphate, and Bone

Bone and skeletal changes develop with alterations in **calcium** and **phosphate metabolism**. These changes begin when the GFR decreases to 25% or less. *Hypocalcemia* is accelerated by impaired renal synthesis of 1,25-dihydroxy-vitamin D3 (calcitriol) with decreased intestinal absorption of calcium. Renal phosphate excretion also decreases and the increased serum phosphate binds calcium, further contributing to hypocalcemia. Acidosis also contributes to a negative calcium balance. Decreased serum calcium level stimulates parathyroid hormone secretion with mobilization of calcium from bone and may cause calcium levels to approach normal. The combined effect of *hyperparathyroidism* and *vitamin D deficiency* can result in renal osteodystrophies (i.e., *osteomalacia* and *osteitis fibrosa* with increased risk for fractures (Ott, 2012). Other consequences of secondary hyperparathyroidism include soft tissue and vascular calcification, cardiovascular disease, and, less commonly, calcific uremic arteriolopathy (Mejía et al., 2011).

3.6 Protein, Carbohydrate, and Fat Metabolism

Protein, carbohydrate, and fat metabolism are altered in chronic kidney disease (CKD). *Proteinuria* and a catabolic state contribute to a negative nitrogen balance. Levels of serum proteins diminish, including albumin, complement, and transferrin, and there is loss of muscle mass. Proteinuria may independently cause renal damage by promoting tubular inflammation and fibrosis (Gorriz & Martinez-Castelao, 2012). The amount of proteinuria is also related to the extent of renal injury and predicts disease progression (Viswanathan & Upadhyay, 2011). Monitoring of proteinuria using the albumin to creatinine ratio among all individuals with CKD who are not receiving chronic dialysis therapy has been recommended as

a quality performance measure for improving patient outcomes (Thorp et al., 2012).

Hyperinsulinemia and glucose intolerance related to insulin resistance are common and may be related to alterations in adipokines that interfere with insulin action and oxidative stress that contribute to renal tubular and vascular injury in both nondiabetic and diabetic CKD (Ikee et al., 2008). Hyperparathyroidism also decreases insulin sensitivity and impairs glucose tolerance. High levels of adiponectin have been associated with increased mortality in CKD (Jia et al., 2012). *Dyslipidemia* is common among individuals with CKD. There is a high ratio of low-density lipoprotein (LDL) to high-density lipoprotein (HDL), high levels of triglycerides, and accumulation of LDL particles with accelerated atherosclerosis and vascular calcification. Uremia causes a deficiency in lipoprotein lipase and decreased hepatic triglyceride lipase. Decreased lipolytic activity results in a reduction in HDL level. Apolipoprotein B concentration is also elevated, thereby accelerating atherogenesis (KD et al., 2011) (Bakris, 2012).

3.7 Cardiovascular System

Cardiovascular disease is a major cause of morbidity and mortality in CKD. Proinflammatory mediators, oxidative stress, altered vitamin D metabolism, and metabolic derangements are significant contributors. Declining erythropoietin production causes anemia, which reduces oxygen delivery to the myocardium. Elevated renin level stimulates the secretion of aldosterone, increasing sodium and water reabsorption. *Hypertension* is the result of excess sodium and fluid volume. *Dyslipidemia* occurs early in CKD. Arterial wall thickness increases with decreased elastic fibers and increased extracellular matrix. Atheromatous plaque and arterial calcification contribute to loss of vessel elasticity and obstruction and are

accelerated by the oxidative stress of CKD. Macrovascular disease is responsible for increased risk for ischemic heart disease, left ventricular hypertrophy, congestive heart failure, stroke, and peripheral vascular disease in individuals with uremia (Bhandari, 2011). Endothelial cell dysfunction and calcium deposits lead to a loss of vessel elasticity and vascular calcification (Briet & Burns, 2012). The resulting vascular disease increases the risk for *ischemic heart disease, left ventricular hypertrophy, congestive heart failure, stroke,* and *peripheral vascular disease* in individuals with uremia. *Pericarditis* can develop from inflammation caused by the presence of uremic toxins. Accumulation of fluid in the pericardial space can compromise ventricular filling and cardiac output.

3.8 Pulmonary System

Pulmonary edema results from fluid overload and congestive heart failure. *Dyspnea* is common in ESKD. Metabolic acidosis can cause Kussmaul respirations.

3.9 Hematologic System

Hematologic alterations include *normochromic normocytic anemia, impaired platelet function,* and *hypercoagulability*. Inadequate production of erythropoietin decreases red blood cell production and is the most significant factor in contributing to anemia. Chronic inflammation, iron deficiency, and decreased half-life of erythrocytes are also contributing factors. Anemia contributes to decreased tissue oxygenation and contributes to progression of kidney disease. Low levels of hemoglobin and symptoms of anemia, such as lethargy, weakness, and dizziness, are common findings. Treatment of anemia includes erythropoiesis stimulating agents (i.e., recombinant human erythropoietin) and intravenous iron (Locatelli

& Del Vecchio, 2011). Disorders of hemostasis in CKD are primarily related to defective platelet aggregation and impaired adhesion of platelets to the vascular endothelium. The consequence is an increased bleeding tendency manifested by bruising, epistaxis and other mucosal bleeding, gastrointestinal bleeding, and cerebrovascular hemorrhage (Kaw & Malhotra, 2006) (Saeed et al., 2011). Adequate dialysis improves platelet function. Alterations of individual clotting factors, fibrin, thrombin, and fibrinolysis contribute to alterations of blood coagulation and can promote a hypercoagulable state and thrombosis with increased risk for myocardial infarction and stroke (Fabbian et al., 2012) (McCullough et al., 2011).

3.10 Immune System

Immune system dysregulation with immune suppression, deficient response to vaccination, and increased risk for infection develops with CKD. Chemotaxis, phagocytosis, antibody production, and cell-mediated immune responses are suppressed (Vaziri et al., 2012). Malnutrition, metabolic acidosis, hyperglycemia, or effects of hemodialysis may amplify immunosuppression.

3.11 Neurologic System

Neurologic symptoms are common and progressive with CKD and are related to uremic toxicity, chronic hyperkalemic depolarization, and anemia (Krishnan & Kiernan, 2007). Symptoms may include headache, drowsiness, pain, sleep disorders, impaired concentration, memory loss, and impaired judgment. Neuromuscular irritation can cause hiccups, muscle cramps, and muscle twitching. In advanced stages of renal failure, symptoms may progress to seizures and coma. Peripheral neuropathies also develop with

impaired sensations, decreased tendon reflexes, muscle weakness, and muscle atrophy, most commonly in the lower extremities.

3.12 Gastrointestinal System

Gastrointestinal complications are common in individuals with CKD. Uremic gastroenteritis can cause bleeding ulcer and significant blood loss. Nonspecific symptoms include anorexia, nausea, vomiting, and constipation or diarrhea. Uremic fetor is a form of bad breath caused by the breakdown of urea by salivary enzymes. Malnutrition is common.

3.13 Endocrine and Reproductive Systems

Endocrine and reproductive alterations develop with progression of CKD. Males and females have a decrease in the levels of circulating sex steroid hormones. Males often experience a reduction in testosterone levels and may be impotent. Oligospermia and germinal cell dysplasia can result in infertility. Females have reduced estrogen levels, amenorrhea, and difficulty maintaining a pregnancy to term. A decrease in libido occurs in both genders (Iglesias et al., 2012) (Nevis et al., 2011). Insulin resistance is common in uremia. Low-grade systemic inflammation and oxidative stress may be contributing factors with increased risk for cardiovascular disease. As CKD progresses the ability of the kidney to degrade insulin is reduced, and the half-life of insulin is prolonged. Individuals with diabetes mellitus and CKD need to carefully manage their insulin dosages.

Low-protein diets and renal replacement therapy improve insulin sensitivity (Chauveau & Aparicio, 2011)(Garg & Williams, 2013). CKD also causes alterations in thyroid hormone metabolism and low thyroid hormone levels and is known as nonthyroidal illness

syndrome (euthyroid sick syndrome). Low-grade inflammation and oxidative stress may be contributing factors (Adler & Wartofsky, 2007). Uremia also reduces conversion of T3 to T4. A low protein, low-phosphorus diet may improve thyroid hormone function (Rosołowska-Huszcz et al., 2005).

3.14 Integumentary System

Skin changes are associated with other complications that develop with CKD. Anemia can cause pallor and bleeding into the skin and results in hematomas and ecchymosis. Retained urochromes manifest as a sallow skin color. Hyperparathyroidism and uremic skin residues (known as uremic frost) are associated with irritation and pruritus with scratching, excoriation, and increased risk for infection (Manenti et al., 2009).

3.15 Evaluation and Treatment

Early screening and evaluation of CKD are based on risk factors, history, presenting signs and symptoms, and diagnostic testing (Fink et al., 2012). Prediction equations are used for estimating GFR from serum creatinine values or creatinine clearance may be completed. Markers of kidney damage include urine protein, particularly albumin, and examination of urine sediment. New biomarkers for predicting progression of CKD are being evaluated (Fassett et al., 2011). Ultrasound, CT scan, or plain x-ray films will show small kidney size. Renal biopsy confirms the diagnosis. Management involves dietary control, including management of protein intake, vitamin D supplementation, sodium and fluid maintenance, potassium restriction, adequate caloric intake, management of dyslipidemias, and erythropoietin as needed (Fouque et al., 2011) (Prabhu et al., 2012). ACE inhibitors or receptor

blockers are often used to control systemic hypertension and provide renoprotection, particularly in the presence of diabetes mellitus (Nicholas et al., 2013) (Van Buren & Inrig, 2012). ESKD related to diabetic nephropathy can be significantly reduced with control of hyperglycemia, hypertension, and hyperlipidemia (Pyram et al., 2012) (O'Toole et al., 2012). ESKD is treated with dialysis, supportive therapy, and renal transplantation.

3.16 Dialysis and Transplantation

Dialysis or renal replacement therapy is indicated when advanced uremia or serious electrolyte imbalances are present. The choice between dialysis and transplantation is dictated by age, related health problems, donor availability, and personal preference. Although transplantation often is the preferred treatment, dialysis plays a critical role as a treatment method for kidney failure. It is life sustaining for persons who are not candidates for transplantation or who are awaiting transplantation. There are two broad categories of dialysis: hemodialysis and peritoneal dialysis.

3.17 Hemodialysis.

The basic principles of hemodialysis have remained unchanged over the years, although new technology has improved the efficiency and speed of dialysis (Fleming, 2011) (Himmelfarb & Ikizler, 2010). A hemodialysis system, or artificial kidney, consists of three parts: a blood delivery system, a dialyzer, and a dialysis fluid delivery system. The dialyzer is usually a hollow cylinder composed of bundles of capillary tubes through which blood circulates, while the dialysate travels on the outside of the tubes. The walls of the capillary tubes in the dialysis chamber are made up of a semipermeable membrane material that allows all molecules except

blood cells and plasma proteins to move freely in both directions—from the blood into the dialyzing solution and from the dialyzing solution into the blood. The direction of flow is determined by the concentration of the substances contained in the two solutions. The waste products and excess electrolytes in the blood normally diffuse into the dialyzing solution. If there is a need to replace or add substances, such as bicarbonate, to the blood, these can be added to the dialyzing solution.

During dialysis, blood moves from an artery through the tubing and blood chamber in the dialysis machine and then back into the body through a vein. Access to the vascular system is accomplished through an external arteriovenous shunt (i.e., tubing implanted into an artery and a vein) or, more commonly, through an internal arteriovenous fistula (i.e., anastomosis of a vein to an artery, usually in the forearm). Heparin is used to prevent clotting during the dialysis treatment; it can be administered continuously or intermittently. Problems that may occur during dialysis, depending on the rates of blood flow and solute removal, include hypotension, nausea, vomiting, muscle cramps, headache, chest pain, and disequilibrium syndrome. Most persons are dialyzed three times each week for 3 to 4 hours. Many dialysis centers provide the option for patients to learn how to perform hemodialysis at home.

3.18 Peritoneal Dialysis

The same principles of diffusion, osmosis, and ultrafiltration that apply to hemodialysis apply to peritoneal dialysis, in which the thin serous membrane of the peritoneal cavity serves as the dialyzing membrane (Almeras & Argilés, 2009)(Fleming, 2011). The procedure is facilitated by the surgical implantation of a silastic catheter into the peritoneal cavity at a point below the umbilicus. The catheter is tunneled through subcutaneous tissue and exits on the side

of the abdomen. The dialysis process involves instilling a sterile dialyzing solution (usually 1 to 3 L) through the catheter over a period of approximately 10 minutes. The solution then is allowed to remain, or *dwell*, in the peritoneal cavity for a prescribed amount of time, during which the metabolic end products and extracellular fluid diffuse into the dialysis solution. At the end of the dwell time, the dialysis fluid is drained out of the peritoneal cavity by gravity into a sterile bag. The osmotic effects of glucose in the dialysis solution account for water removal. Peritoneal dialysis can be performed at home or in a dialysis center and can be carried out by continuous ambulatory peritoneal dialysis (CAPD), continuous cyclic peritoneal dialysis (CCPD), or nocturnal intermittent peritoneal dialysis (NIPD)—all with variations in the number of exchanges and dwell times (Kopple, 2001) .

Individual preference, manual ability, lifestyle, knowledge of the procedure, and physiologic response to treatment are used to determine the type of dialysis that is used. The most common method is CAPD, a self-care procedure in which the person exchanges the dialysate four to six times a day. In CCPD, exchanges usually are performed at night, with the person connected to an automatic cycler. In the morning, with the last exchange remaining in the abdomen, the person is disconnected from the cycler and goes about his or her usual activities. In NIPD, the person is given approximately 10 hours of automatic cycling each night, with the abdomen left dry during the day. Potential problems with peritoneal dialysis include infection, catheter malfunction, dehydration caused by excessive fluid removal, hyperglycemia, and hernia. The most serious complication is infection, which can occur at the catheter exit site, in the subcutaneous tunnel, or in the peritoneal cavity (i.e., peritonitis).

Table 3.2 Advantages, disadvantages, and dialysis prescription for end-stage renal disease

Advantages, disadvantages and dialysis prescription for end-stage renal disease

	PERITONEAL DIALYSIS	HEMODIALYSIS
Access	Abdominal wall insertion of plastic catheter into the peritoneum Limitations: swimming and bathing can be contraindicated. Previous abdominal surgery can be a contraindication; rarely, a patent pleuro-peritoneal canal exists	Arteriovenous fistula, usually in the forearm
Timing	Daily exchanges, either every 6 hours (CAPD), or attached to an overnight (continuous) cycling machine (8 hours) (CCPD); no non-dialysis days	5–7 hours every 2nd or 3rd day; in some circumstances, daily or overnight hemodialysis can be offered (e.g. pregnancy); some non-dialysis days
Complications	Peritonitis (usually staphylococcal) Poorer exchange rates over time Peritoneal sclerosis in the long term	Bleeding from insertion sites Fistula aneurysm formation Recirculation or 'steal' phenomenon Poor flow rates and technical difficulties Fistula thrombosis or infection Progressive neurological disease
Compelling indications		Pregnancy Congestive cardiac failure Unstable coronary artery disease
Other considerations	Bulky home stores	Adequate space for machines at home Adequate plumbing, good-quality water supply
2-year patient survival	77%	60–80%
2-year technique survival	64%	60–80%
CAPD, continuous ambulatory peritoneal dialysis; CCPD, continuous cycling peritoneal dialysis.		

Source : Essentials of Internal Medicine (2014, Churchill Livingstone) - Nicholas J. Talley, Brad Frankum, David Currow

3.19 Transplantation

Greatly improved success rates have made kidney transplantation the treatment of choice for many patients with CKD. The availability of donor organs continues to limit the number of transplantations performed each year. Donor organs are obtained from cadavers and living related donors (e.g., parent, sibling). Transplants from living unrelated donors (e.g., spouse) have been used in cases of suitable ABO blood type and tissue compatibility. The success of transplantation depends primarily on the degree of histocompatibility, adequate organ preservation, and immunologic management. Maintenance immunosuppressive therapy plays an essential role in controlling T- and B-cell activation.

CHAPTER 4

NEPHROTIC AND NEPHRITIC SYNDROMES

Nephrotic syndrome is the excretion of 3.0 g or more of protein in the urine per day, hypoalbuminemia (less than 3.0 g/ dl), and peripheral edema. Nephrotic syndrome is characteristic of glomerular injury. *Primary causes of nephrotic syndrome* include minimal change disease (lipoid nephrosis), membranous glomerulonephritis, and focal segmental glomerulosclerosis. *Secondary forms of nephrotic syndrome* occur in systemic diseases including diabetes mellitus, amyloidosis, systemic lupus erythematosus, and Henoch-Schönlein purpura. Nephrotic syndrome also is seen with certain drugs, infections, malignancies, and vascular disorders. Familial forms of nephrotic syndrome result from genetic defects that affect the function and composition of the glomerular capillary wall (i.e., Alport syndrome with alterations in basement membrane type IV collagen) (Cosgrove, 2012) . It often signifies a more serious prognosis when present as a secondary complication. Nephrotic syndrome is more common in children than in adults.

In **nephritic syndrome,** the presenting symptom is hematuria (usually microscopic) and red blood cell casts are present in the urine in addition to proteinuria, which is not severe. This syndrome is caused by increased permeability of the glomerular filtration membrane with pore sizes large enough to allow the passage of red

blood cells and protein. Nephritic syndrome is associated with postinfectious glomerulonephritis, rapidly progressive (crescentic) glomerulonephritis, IgA nephropathy (see Chapter 8 for types of immunoglobulins), lupus nephritis, and diabetic nephropathy. The pathophysiology is related to immune injury of the glomerulus as previously described and can occur simultaneously with nephrotic syndrome. Hypertension, uremia, and oliguria occur in advanced stages of disease. The symptoms and treatment are similar to those for nephrotic syndrome (Khanna, 2011).

4.1 Pathophysiology

Disturbances in the glomerular basement membrane (GBM) and podocyte injury lead to increased permeability to protein and loss of electrical negative charge (Galle & Labejof, 2011). Loss of plasma proteins, particularly albumin and some immunoglobulins, occurs across the injured glomerular filtration membrane. Sustained proteinuria can result in the release of inflammatory mediators and cytokines by tubular cells with influx of leukocytes resulting in progressive glomerulosclerosis and renal fibrosis (Siddall & Radhakrishnan, 2012).

Hypoalbuminemia results from urinary loss of albumin combined with a diminished synthesis of replacement albumin by the liver. Albumin is lost in the greatest quantity because of its high plasma concentration and low molecular weight. Decreased dietary intake of protein from anorexia or malnutrition or accompanying liver disease may also contribute to lower levels of plasma albumin. Loss of albumin stimulates lipoprotein synthesis by the liver and hyperlipidemia. Loss of immunoglobulins may increase susceptibility to infections. Sodium retention also is associated with

nephrotic syndrome contributing to the development of edema and

ascites. The exact mechanism is unknown but the site of retention is the distal tubules and collecting ducts (Svenningsen et al., 2012).

4.2 Clinical Manifestations

Many clinical manifestations of nephrotic syndrome are related to loss of serum proteins and retention of sodium. They include edema, hyperlipidemia, lipiduria, vitamin D deficiency, and hypothyroidism (De Seigneux & Martin, 2009) (Iglesias & Díez, 2009). Vitamin D deficiency is related to loss of serum transport proteins and decreased vitamin D activation by the kidney. Hypothyroidism can result from urinary loss of thyroid-binding protein and thyroxine but there may be no symptoms. Alterations in coagulation factors cause hypercoagulability and may lead to thromboembolic events, particularly in young adults (Kerlin et al., 2012).

4.3 Evaluation and Treatment

Nephrotic syndrome is diagnosed when the protein level in a 24-hour urine collection is greater than 3.0 g. Serum albumin level decreases (to less than 3 g/dl), and concentrations of serum cholesterol, phospholipids, and triglycerides increase. Fat bodies may be present in the urine. The specific pathologic condition is identified by renal biopsy. Nephrotic syndrome is commonly treated with a normal protein (i.e., 1 g/kg body weight/day) low-fat diet, salt restriction, diuretics, immunosuppression, and heparinoids. When diuretics are used, care must be taken to observe for hypovolemia and hypokalemia or potassium toxicity in the presence of renal insufficiency. Aldactone may be combined with loop diuretics to suppress aldosterone activity to conserve potassium. Corticosteroids or cyclophosphamide may be particularly effective for the initial

treatment of steroid-dependent nephrotic syndrome in children. Immunosuppressive drugs and angiotensin-converting enzyme inhibitors are used with steroid-resistant nephrotic syndrome (Lombel et al., 2013) (Ulinsky & Aoun, 2012).

CHAPTER 5

KIDNEY STONES

Calculi, or **urinary stones (urolithiasis),** are masses of crystals, protein, or other substances that are a common cause of urinary tract obstruction in adults. They can be located in the kidneys, ureters, and urinary bladder. The prevalence of stones in the United States is approximately 6% in women and 15% in men, and is more common in whites (Sakhaee et al., 2012)(Curhan, 2007). The recurrence rate is approximately 30% to 50% within 5 years (Chandhoke, 2007).

The risk of urinary calculi formation is influenced by a number of factors, including age, gender, race, geographic location, seasonal factors, fluid intake, diet, occupation, genetic predisposition, and other conditions including urinary tract infection, hypertension, atherosclerosis, metabolic syndrome, obesity, and diabetes (Sas, 2011). Most persons develop their first stone before age 50 years. Geographic location influences the risk of stone formation because of indirect factors, including average temperature, humidity, and rain fall, and their influence on fluid and dietary patterns. Persons who regularly consume an adequate volume of water and those who are physically active are at reduced risk when compared with people who are inactive or consume lower volumes of fluid. Most kidney stones are unilateral and are a risk factor for chronic kidney disease and an increased risk for myocardial infarction (Rule et al., 2010)(Rule et al., 2011).

Urinary calculi can be classified according to the primary minerals (salts) that comprise the stones. The most common stone typesinclude calcium oxalate or phosphate (70% to 80%), struvite (magnesium, ammonium, and phosphate) (15%), and uric acid (7%). Cystine stones are rare, less than 1%. Less common stone elements include cystine, 2,8-dihydroxyadeninuria (a rare genetic disorder that increases risk of xanthine stones), triamterene (a diuretic), and indinavir (a protease inhibitor used in management of human immunodeficiency virus [HIV] infection). Urinary calculi also can be classified according to location and size. *Staghorn calculi* are large and fill the minor and major calyces. *Non-staghorn calculi* are of variable size and are located in the calyces, in the renal pelvis, or at different sites along the ureter.

5.1 Pathophysiology

Renal calculus formation is complex and related to: (1) supersaturation of one or more salts in the urine, (2) precipitation of the salts from a liquid to a solid state (crystals), (3) growth through crystallization or agglomeration (sometimes called aggregation), and (4) the presence or absence of stone inhibitors (Evan, 2010). *Supersaturation* is the presence of a higher concentration of a salt within a fluid (in this case, the urine) than the volume is able to dissolve to maintain equilibrium. Human urine contains many positively and negatively charged ions capable of *precipitating* from solution and forming a variety of salts. The salts form crystals that are retained and grow into stones.

Crystallization is the process by which crystals grow from a small *nidus* or nucleus to larger stones in the presence of supersaturated urine. Although supersaturation is essential for free stone formation, the urine need not remain continuously supersaturated for a calculus to grow once its nidus has precipitated

from solution. Intermittent periods of supersaturation after the ingestion of a meal or during times of dehydration are sufficient for stone growth in many individuals. In addition, the apical papillae have interstitial sites where hydroxy apatite deposits (Randall plaque) become exposed and serve as sites for calcium oxalate stone formation (but not calcium phosphate stone formation) (Bagga et al., 2013).

Matrix is an organic material (i.e., mucoprotein) in which the components of a kidney stone are embedded (Evan, 2010). The pH of the urine also influences the risk of precipitation and calculus formation. An alkaline urinary pH significantly increases the risk of calcium phosphate stone formation, whereas acidic urine increases the risk of a uric acid stone. Cystine and xanthine precipitate more readily in acidic urine.

Stone or *crystal growth inhibiting substances,* including potassium citrate, pyrophosphate, and magnesium, are capable of crystal growth inhibition, thereby reducing the risk of calcium phosphate or calcium oxalate precipitation in the urine and preventing subsequent stone formation. Retention of *crystal particles* occurs primarily at the papillary collecting ducts. Although most crystals are flushed from the tract through antegrade urine flow, urinary stasis, anatomic abnormalities, or inflamed epithelium within the urinary tract may prevent prompt flushing of crystals from the system, thus increasing the risk of calculus formation. The size of a stone determines the likelihood that it will pass through the urinary tract and be excreted through micturition (Lingeman & Lifshitz, 2002). Stones smaller than 5 mm have about a 50% chance of spontaneous passage, whereas stones that are 1 cm have almost no chance of spontaneous passage. Nevertheless, the person with ureteral dilation from the previous passage of a stone may be able to

excrete larger stones when compared with the person experiencing an initial obstructing calculus.

Calcium stones (urolithiasis) account for 70% to 80% of all stones requiring treatment. Calcium oxalate accounts for about 80% of these stones and calcium phosphate about 15% (Coe et al., 2011). Both genetic and environmental factors may increase susceptibility. Most affected individuals have *idiopathic calcium oxalate urolithiasis (ICOU),* a condition whose exact etiology has not yet been defined. Stones can form freely in supersaturated urine or detach from interstitial sites of formation (Tiselius, 2011). Hypercalciuria, hyperoxaluria, hyperuricosuria, hypocitraturia, mild renal tubular acidosis, crystal growth inhibitor deficiencies, and alkaline urine are associated with calcium stone formation (Sakhaee et al., 2012)(Wagner & Mohebbi, 2010). Hypercalciuria and hyperoxaluria are usually attributable to intestinal hyperabsorption and less commonly to a defect in renal calcium reabsorption. Hyperparathyroidism and bone demineralization associated with prolonged immobilization are also known to cause hypercalciuria.

Struvite stones primarily contain magnesium-ammoniumphosphate as well as varying levels of matrix. Matrix forms in an alkaline urine and during infection with a urease-producing bacterial pathogen, such as a *Proteus, Klebsiella,* or *Pseudomonas.* Struvite calculi may grow quite large and branch into a staghorn configuration **(staghorn calculus)** that approximates the pelvicaliceal collecting system. Women are at greater risk for struvite stones because they have an increased incidence of urinary tract infection. Uric acid is primarily a product of biosynthesis of endogenous purines and is secondarily affected by consumption of purines in the diet. Persons who excrete excessive uric acid in the urine, such as those with gouty arthritis, are at particular risk for **uric acid stones.** A consistently acidic urine greatly increases this risk.

Cystine and xanthine are amino acids that precipitate more readily in acidic urine.

Cystinuria and *xanthinuria* are genetic disorders of amino acid metabolism, and their excess in urine can cause **cystinuric,** or **xanthine, stone** formation in the presence of a low urine pH of 5.5 or less.

5.2 Clinical Manifestations

Renal colic, described as moderate to severe pain often originating in the posterior hypochondrium (flank) and radiating to the groin, usually indicates obstruction of the renal pelvis or proximal ureter. Colic that radiates to the lateral flank or lower abdomen typically indicates obstruction in the midureter, and bothersome lower urinary tract symptoms (urgency, frequent voiding, urge incontinence) indicate obstruction of the lower ureter or ureterovesical junction. The pain can be severe and incapacitating and may be accompanied by nausea and vomiting. Gross (visible blood in the urine) or microscopic hematuria (three or more red blood cells per high power microscopic field) may be present.[18]

5.3 Evaluation and Treatment

The evaluation and diagnosis of urinary calculi are based on presenting symptoms and history combined with a focused physical assessment, imaging studies, and possibly a functional study of renal pelvic and ureteral pressures (Sakhaee et al., 2012). The history queries dietary habits; the age of the first stone episode; stone analysis; and presence of complicating factors, including recurrent urinary tract infection, hyperparathyroidism, or recent gastrointestinal or genitourinary surgery. Urinalysis (including pH) is obtained and a 24-hour urine is completed to identify calcium

oxalate, citrate, and other significant constituents. In addition, every effort is made to retrieve and analyze calculi that are passed spontaneously or retrieved through aggressive intervention. Additional tests are obtained in selected individuals, such as those with suspected hyperparathyroidism or cystine or uric acid stones, in order to diagnose and manage underlying metabolic disorders. Imaging of kidney stones includes plain abdominal radiography, ultrasound, intravenous pyelogram, computed tomography, and magnetic resonance imaging (Mandeville et al., 2011).

The goals of treatment are to manage acute pain, promote stone passage, reduce the size of stones already formed, and prevent new stone formation. The components of treatment include: (1) administering parenteral and/or oral analgesics for acute pain, (2) providing medical therapy to promote stone passage (alpha antagonists or calcium channel blockers), (3) reducing the concentration of stone-forming substances by increasing urine flow rate with high fluid intake, (4) decreasing the amount of stone-forming substances in the urine by decreasing dietary intake or endogenous production or by altering urine pH (Ortiz-Alvarado et al., 2011), and (5) removing stones using percutaneous nephrolithotomy, ureteroscopy, or ultrasonic or laser lithotripsy to fragment stones for excretion in the urine (Aboumarzouk et al., 2012) (Amer et al., 2012). Obstructing kidney stones with a suspected proximal urinary tract infection are urologic emergencies requiring emergent decompression and antibiotic (Graham et al., 2011).

CHAPTER 6

BENIGN PROSTATIC HYPERPLASIA

Benign prostatic hyperplasia (BPH), also called **benign prostatic hypertrophy,** is the enlargement of the prostate gland. Because the major prostatic changes are caused by hyperplasia, not hypertrophy, benign prostatic hyperplasia is the preferred term. This condition becomes problematic as prostatic tissue compresses the urethra, where it passes through the prostate, resulting in frequency of lower urinary tract symptoms. The prevalence among U.S. men 60 years and older is about 50% and among men 70 years or older 90% (Platz et al., 2012). BPH is common and involves a complex pathophysiology with several endocrine and local factors and remodeled microenvironment. Its relationship to aging is well documented. At birth the prostate is pea sized, and growth of the gland is gradual until puberty.A period of rapid development continues until the third decade of life, when the prostate reaches adult size. Around 40 to 45 years of age, benign hyperplasia begins and continues slowly until death. Although dihydrotestosterone (DHT) is necessary for normal prostatic development, its role in BPH remains unclear. Among all androgen-metabolizing enzymes within the human prostate, 5α-reductase is the most powerful. This reductase corresponds to an age-dependent DHT level. Therefore, although 5α-reductase and DHT decrease with age in the epithelium, they remain relatively constant in the stroma of the prostate gland.

6.1 Pathogenesis

Current causative theories of BPH focus on levels and ratios of endocrine factors such as androgens, estrogens, gonadotropins, and prolactin and changes in the balance between autocrine/paracrine growth-stimulatory and growth inhibitory factors. These factors include insulin-like growth factors (IGFs), epidermal growth factor, nerve growth factor, fibroblast factors, IGF binding proteins, and transforming growth factor-beta (TGF-β) (Timms & Hofkamp, 2011). Aging and circulating androgens are associated with BPH and enlargement. These factors are predisposed as disrupting the *balance* of growth factor signaling pathways and stromal/ epithelial interactions creating a growth-promoting and tissue remodeling microenvironment. However, BPH is a multifactorial disease, and not all men respond well to available treatments, suggesting factors other than androgens are involved. Testosterone, the primary circulating androgen in men, also can be metabolized through CYP19/aromatase into the potent estrogen, estradiol-17β. The prostate is an estrogen target tissue and estrogens directly and indirectly affect growth and differentiation of prostate. The precise role of endogenous and exogenous estrogens in directly affecting prostate growth and differentiation in the context of BPH is an understudied area.

Estrogens and selective estrogen receptor modulators have been shown to promote or inhibit prostate proliferation, signifying potential roles in BPH (Nicholson & Ricke, 2011). Taken together these interactions lead to an increase in prostate volume. The remodeled stroma promotes local inflammation with altered cytokine, reactive oxygen/nitrogen species, and chemo attractants (Chughtai et al., 2011). The resultant increased oxygen demands of proliferating cells causes a local hypoxia that induces angiogenesis and changes to fibroblasts. Functional and phenotypic changes

(transdifferentiation) of fibroblasts to the myofibroblasts is a hallmark of the remodeled micro enviroment (Sampson et al., 2008). BPH begins in the periurethral glands, which are the inner glands or layers of the prostate. The prostate enlarges as nodules form and grow (nodular hyperplasia) and glandular cells enlarge (hypertrophy). The development of BPH occurs over a prolonged period, and changes within the urinary tract are slow and insidious.

6.2 Clinical Manifestations

As nodular hyperplasia and cellular hypertrophy progress, tissues that surround the prostatic urethra usually compressit but not always cause **bladder outflow obstruction.** These symptoms are sometimes called the spectrum of lower urinary tract symptoms (LUTS). Symptoms include the urge to urinate often, some delay in starting urination, and decreased force of the urinary stream. As the obstruction progresses, often over several years, the bladder cannot empty all the urine and the increasing volume leads to long-term urine retention. The volume of urine retained may be great enough to produce uncontrolled "overflow incontinence" with any increase in intra-abdominal pressure. At this stage the force of the urinary stream is significantly reduced, and much more time is required to initiate and complete voiding. Hematuria, bladder or kidney infection, bladder calculi, acute urinary retention hydroureter, hydronephrosis, and renal insufficiency are common complications (Bachmann & Rosette, 2012). Some men initially have signs of uremia and renal failure. On digital rectal examination the hyperplastic prostate is a soft or firm enlargement with smooth mucosal surface and no discernible distinction between lobes; asymmetry is common. The palpated prostate does not always reflect the degree of BPH because a substantial portion of the enlargement

is intravesicular (Cooperberg et al., 2012). Thirty percent of men with mild to moderate symptoms improve with watchful waiting.

6.3 Evaluation And Treatment

Diagnosis is made from a medical history, physical exam, and laboratory tests including urinalysis. Careful review of symptoms is necessary. Digital rectal examination (DRE) and PSA are conducted to determine hyperplasia. PSA alone, however, cannot determine whether symptoms are caused by BPH because PSA is elevated in both BPH and prostate cancer. Annual DREs are used to screen men older than 40 years of age for BPH, sooner in high-risk men (Kapoor, 2012). If marked enlargement, moderate to severe symptoms, or complications are present, transrectal ultrasound (TRUS) is used to determine bladder and prostate volume and residual urine. Urinalysis, serum creatinine and blood urea nitrogen, uroflowmetry, post void residual (PVR) urine, pressure-flow study, cystometry, and cystourethroscopy are used to determine kidney and bladder function (Bachmann & Rosette, 2012). BPH has been treated successfully with drugs. α1-Adrenergic blockers (prazosin and tamsulosin) are used to relax the smooth muscle of the bladder and prostate. Antiandrogen agents, such as finasteride (Proscar), selectively block androgens at the prostate cellular level and cause the prostate gland to shrink (Kapoor, 2012). By shrinking the prostate, these drugs have been shown to improve BPH-related symptoms and reduce the risk of future urinary retention and BPH-related surgery. α1- Adrenergic blockers do not affect PSA and have no effect on prostate cancer risk. However, antiandrogen agents lower PSA by 50% after 6 months of therapy (Kapoor, 2012). Newer minimally invasive procedures include interstitial laser therapy, transurethral radiofrequency procedure (TUNA), cooled Thermo Therapy and prostate artery embolization. When necessary, the hyperplastic tissue may be

removed surgically to prevent the serious consequences of urethral obstruction. A permanent indwelling catheter is inserted if the individual cannot tolerate surgery.

6.4 Diagnostic Studies

a) Urinalysis: uses a dipstick, provides info about kidney function, and helps dx other diseases like diabetes
b) Urine culture: determines whether bacteria is present in the urine, as well as their strains and concentration, also ID antimicrobial therapies that are best suited for particular strain
c) Ultrasonography: noninvasive procedure that uses sounds waves to detect abnormalities of internal tissues and organs. ID of fluid accumulation, massess, congenital malformations, change in organ size, and obstructions. Requires a full bladder
d) CT and MRI: noninvasive, provides cross-sectional views of the anatomy of kidneys and urinary tract, used to eval GU masses, nephroliathiasis, chronic renal infections, renal or UT trauma, metastic disease, soft tissue abnormalities. Occasionally uses IV radiopaque contrast.
   NC: before MRI all metal should be removed, avoid alcohol, caffeine, and smoking for at least 2 hours and food for at least 1 hour prior to scan
e) Nuclear scans: requires injection of radioisotope, it is then monitored as it moves through the blood vessels of the kidneys, provides information about kidney perfusion, used to ID acute and chronic renal failure, renal masses, and blood flow before and after kidney transplantation, AFTER pt encouraged to drink fluids to excrete dye.
f) IV urography: radiopaque contrast administered IV, shows the kidneys, ureter, and bladder via x-ray as the dye moves through the upper and then the lower urinary system, may be

used as initial assessment of suspected urologic conditions, especially leisons in the kidneys and ureters, provides approximate estimate of renal function.

g) Retrograde pyelography: Catheters advances through the ureters into the renal pelvis by means of cystoscopy. Contrast agent is then injected, usually performed when IV urography provides inadequate visualization of the collecting systems. COMPLICATIONS: infection, hematuria, perforation of the ureter. Used infrequently.

h) Cystography: aids in evaluating vesicoureteral reflux (backflow of urine from the bladder into 1 or both ureters) and assessing bladder injury. Cath is inserted into the bladder and a contrast agent is instilled to outline the bladder wall. Can be performed with simultaneous pressure recordings inside the bladder.

CHAPTER 7

DIAGNOSTIC TEST

7.1 Kidney Biopsy

a) Brush biopsy: provides specific info when abnormal xray findings of the ureter or renal pelvis reaise questions about whether a defect is a tumor, a tone, a blood clot, or an artifact, the leison is brushed back and forth to obtain cells and surface tissue fragments for histologic analysis

b) Kidney biopsy: help dx and eval extent of kidney disease, indications: unexplained acute renal failure, persistent proteinuria or hematuria, transplant rejection or glomerularpathies. before: coagulation studies obtained.

c) CONTRA: bleeding tendencies, uncontrolled HTN, a solitary kidney, and morbid obesity. Pt may fast 6-8 hours prior, IV line established, urine specimen obtained for comparison.

d) NC: IV fluids, px clot formation, urine may contain blood for 24-48hrs post.

7.2 Renal Angiography

a) Provides image of renal arteries, femoral is pierced with needle and cath is threaded through the femoral and iliac arteries into the aorta or renal artery, contrast is injected, used to eval renal blood flow in suspected trauma, to differentiate renal cysts

from tumors, and to eval HTN, used preop for renal transplantation.

b) NC: laxative may be rx preop for unobstructed x-rays, peripheral pulse sites are marked, after VS are monitored until stable, assess for swelling or hematoma at site, cold compresses may be used for edema or pain

c) Complications: hematoma formation, arterial thrombosis or dissection, false aneurysm formation, and altered renal function.

7.3 Urologic Endoscopic Procedures

a) Can be performed using cystoscope inserted into urethra or percutaneously through a small incision.

b) Used for direct visualization of the urethra and bladder

c) Small ureteral catheters can be passed through the cystoscope for assessment of the ureters and the pelvis of each kidney.

d) Allows to obtain urine specimen from each kidney to eval function, cup forceps can be inserted through the cystoscope for biopsy. Calculi may be removed from the urethra, bladder, and ureter.

e) If lower cystoscopy pt is usually conscious and is no more uncomfortable than catheterization.

f) Lidocaine may be administered to minimize post procedure discomfort.

g) If upper a sedative agent may be administered, usually general anesthesia.

NC: upper is NPO for several hours prior to procedure. Goal is to minimize discomfort. Burning upon voiding, blood tinged urine, and urinary frequency from trauma are expected. Apply moist heat and warm sitz baths to relieve pain and relax muscles. Antispasmodic may be rx to releive urinary retention, intermittent

cath may be needed for a few hours after exam. Monitor for S&S of UTI.

7.4 Intravenous Pyelogram

Intravenous pyelography (IVP), or intravenous urography, is a diagnostic test that involves the administration of intravenous contrast and X-ray imaging of the urinary tract. The iodinated contrast flows through the renal vasculature and filtered into the collecting system highlighting the anatomic structures on the X-ray image. It is often useful for the evaluation of hematuria, and renal stone disease, and as a follow-up after the intervention. The urographic imaging sequence is designed to depict specific parts of the urinary tract optimally. Portions of the urinary system appear opaque when filled with contrast material 1. Accurate conclusions from the IVP are feasible only when the technique, limitations, and basic rules of interpretation are known.

7.4.1 Intravenous Pyelogram Purpose

This test lets your doctor see the size and shape of your bladder, kidneys, and ureters, and how well they're working. They can spot blockages in your urinary tract caused by:

a) Kidney stones
b) Enlarged prostate
c) Tumors in the kidney, ureters, or bladder
d) Kidney cysts
e) Scarring, either from surgery or a urinary tract infection
f) Congenital problems in the urinary tract, such as medullary sponge kidney.
g) IVP images can give your doctor enough detailed information to treat a blockage with medication. Otherwise, you may need surgery. While IVP used to be the go-to procedure for

diagnosing urinary tract problems, it's largely been replaced by ultrasound and CT scans.

An intravenous pyelogram isn't a good choice for everyone. Don't get the procedure if: you're allergic to iodine or contrast dye. You have kidney disease. You're pregnant or may be pregnant. Your doctor will most likely choose a different test, because X-rays use a small burst of radiation. Infants and children rarely get IVPs.

7.4.2 Intravenous Pyelogram Risks

Most of the time, an intravenous pyelogram is safe with no complications. But there are side effects and some risks. Side effects

a) You'll feel a sting as the technician injects the contrast material into your hand or arm.
b) You may feel itchy or become flushed as the contrast material moves through your body.
c) You might have a salty or metallic taste in your mouth.
d) You could have a brief headache.
e) You may feel nauseated.
f) These side effects are common and normally go away within a couple of minutes.

7.4.3 Risks and Contraindications

Risks associated with an intravenous pyelogram are minor, but there can be complications, and it is almost always because of the contrast media used (X-ray dye). Intravenous pyelography is not the only type of medical test that uses contrast media. Dye is used in many medical tests and most of them use quite a bit more of it than an intravenous pyelogram does. Modern versions of X-ray dye are very safe. A very small number of all patients getting contrast media experience some sort of reaction to it. These reactions are usually

very minor and are divided into two categories: allergy-like and physiologic.[2]

7.4.4 Intravenous Pyelogram Preparation

Before you have the test, let your doctor know if you're pregnant or have any medical conditions, if you have allergies, and if you're taking any prescription or over-the-counter medicines. If you take any of these, you might need to stop before your procedure: Aspirin, Blood thinners, Metformin, a diabetes medicine. The doctor may ask you to take mild laxative the night before the IVP and tell you not to eat or drink after midnight.

7.4.5 Preparing the patient

a) Fasting is recommended for the patient before the procedure.
b) The patient must empty their bladder before the procedure.
c) Mild laxatives may be prescribed.
d) Explain the procedure to the patient.
e) Carefully note the history of patient's allergies, comorbidities, previous illnesses, and drug history.
f) Ask the patient to remove all jewelry and other metal objects before the procedure.
g) If the patient is a female, ensure that she is not pregnant at the time of the procedure. If she is pregnant, take precautionary measures to shelter the fetus from radiation exposure.
h) This examination is usually performed on an outpatient basis.

7.4.6 Intravenous Pyelogram Procedure

You'll probably change into a hospital gown. A lab technician will inject a liquid called a contrast material into your hand or arm through an IV. The dye travels through your bloodstream to your kidneys and urinary tract. You'll lie still on a table as the tech takes

the X-rays. You may be asked to turn from side to side and hold different positions.

The IVP shows the urinary tract in action as your kidney begins to empty into the ureters. These are the tubes that carry urine to the bladder. The iodine will show up as bright white on the film. Dye that doesn't move or moves too slowly shows where the blockages are. The images also may show that your kidney, bladder, or ureter isn't working as well as it should. Near the end of the exam, you'll be asked to pee. This lets your radiologist get a picture of your bladder after it empties.

An IVP usually takes less than 1 hour. If your kidneys work more slowly, the test can last up to 4 hours. You should be able to go back to your normal diet and activities afterward. The doctor may tell you to drink more fluids than normal to flush the contrast dye from your body.

7.4.7 Allergic reactions

In rare cases, you may have an allergic reaction to the contrast material, or dye. That will cause: itching that lasts longer than a few minutes, hives, these symptoms can be treated with medication.

7.4.8 Serious reaction

It's less common, but possible, to have a serious allergic reaction. That can cause: shortness of breath, swelling in your throat or elsewhere, low blood pressure, cardiac arrest, tell your radiologist right away if you have any symptoms.

You're more likely to have an allergic reaction to the dye if you have: Allergies or asthma Congestive heart failure, Diabetes, If you have kidney disease, there's a chance the contrast material, or dye, could cause further kidney damage. As with any X-ray, your

body is exposed to radiation that can cause cancer. But the level is low in an IVP.

7.4.9 Intravenous Pyelogram Results

A radiologist will analyze the images and send a report to your doctor, who'll share the results with you. Abnormal results could mean you have: kidney stones, enlarged prostate, tumor or cyst in your urinary tract, Structural problems with your kidneys, bladder, or ureters, Scarring or other damage in your urinary tract.

An intravenous pyelogram is a medical imaging test that uses contrast media (also known as dye) injected into the veins to help see the urinary system clearly on an X-ray. An intravenous pyelogram is sometimes abbreviated as "IVP." It is also known as intravenous urography, or an intravenous urogram, and can be abbreviated as "IVU."

An intravenous pyelogram is used to see the structures and outlines of the kidneys, ureters, and bladder. With better visibility, healthcare providers can see abnormalities, such as scarring, tumors, or kidney stones.1 The practitioner might order an intravenous pyelogram as an early test to help diagnose causes of certain signs and symptoms, such as abdominal or flank pain, pain during urination, difficulty urinating, or blood in urine. An intravenous pyelogram can assist healthcare providers in identifying, among other things: Kidney or bladder stones, Tumors or cysts in the kidneys, ureters, or bladder, Scarring after urinary surgery or trauma, Enlarged prostate gland, Congenital kidney defects, such as medullary sponge kidney.

In the past, intravenous pyelograms were the most common way for practitioners to see kidney stones and other objects in the urinary tract. It has become less commonly used since the development of renal ultrasound and CT technology that can clearly

show the urinary tract. Renal ultrasound does not require the use of contrast media, which can lead to complications (see below). A CT urogram or CT IVP requires using IV contrast and provides greater detail.

7.4.10 Allergy-Like Reactions to Dye

A patient doesn't have to be allergic to contrast media in order to exhibit allergy-like reactions to it. While the reasons aren't completely clear, sometimes dyes will trigger a histamine release just like an allergy. Allergy-like reactions are graded as mild, moderate, or severe:2

Mild reactions may include localized hives, swelling, or itching at the intravenous site, an itchy and scratchy throat, sneezing, conjunctivitis, and nasal congestion. Moderate reactions may include hives and redness spread out away from the intravenous site, swelling of the face, tightness of the throat, possible wheezing, and little or no difficulty breathing. Patients with moderate reactions maintain stable vital signs.

Severe allergy-like reactions mimic anaphylaxis, including shortness of breath, swelling of the face and other areas, and anaphylactic shock, which could include decreased blood pressure. To decrease the chances of an allergy-like reaction, your healthcare provider may give you steroids at several intervals starting the night before the test, and an antihistamine such as diphenhydramine about an hour before the intravenous pyelogram begins.

In addition to allergy-like reactions to contrast media, there are also potential physiologic side effects. These include: nausea, headache, flushing, elevated blood pressure, altered taste (sometimes described as a metallic taste in the mouth) The good news is that physiologic reactions are not life-threatening. The bad news is that

there's nothing your healthcare provider can do to prevent them the way they can for allergy-like reactions.

7.5 Renal Function and Contrast Media

Another rare risk factor of intravenous contrast media is Contrast Induced Nephrotoxicity (CIN). How CIN happens is not fully understood, but there are certain people who are at increased risk:3 Patients over 60 years old, History of dialysis, kidney transplant, single kidney, renal cancer, or renal surgery, History of high blood pressure requiring treatment, History of diabetes mellitus, History of taking metformin or drugs containing metformin combinations, Cardiovascular disease, Anemia, Multiple myeloma. Patients who are dehydrated or who have received intravenous dye in the last 24 hours are also at an increased risk for CIN. Talk to your healthcare provider before getting an intravenous pyelogram if you have any of the risks above.

7.5.1 Extravasation

If the contrast media leaks out of the vein and gets into the surrounding tissue, it's known as extravasation. It is possible to have a local reaction to the dye in that case. If you feel swelling or pain at the site of the intravenous administration, be sure to tell the medical professional performing the test.[2]

7.5.2 Before the Test

Your healthcare provider will give you specific instructions for the intravenous pyelogram. Usually, you will be asked not to eat or drink after midnight on the evening before your test. You might have to take a laxative the night before your intravenous pyelogram to help clear out your colon. That makes it easier to see your urinary system on the images. The practitioner prescribes the test, makes

sure to tell them if you are pregnant, have any allergies (especially to iodine), or have ever had a reaction to contrast media (dye).

Timing. Give yourself six hours for the test. The preparation, including receiving an antihistamine and the contrast medium, will take about an hour. The pyelogram will take anywhere from one to four hours.

Location. An intravenous pyelogram is performed at an imaging center, which might be at a hospital.

What to Wear. You'll most likely be asked to change into a gown, so wear something comfortable and easy to change out of.

What to Bring. There is a bit of downtime as you are waiting for some parts of the process to take place. Consider bringing something to read.

During the Test. When you arrive for your test, check in at the desk and you'll be sent to change into a gown.

7.5.3 Pre-Test

A nurse will start an intravenous line and probably administer an antihistamine. Typically, you will wait in a room until the medication has had time to circulate.

Throughout the Test. You'll start out by getting some X-rays before the contrast medium is administered. This will be done on an X-ray table. You will probably be asked to change positions a few times. How many times you have to switch positions depends on the reason for the test and what images the healthcare provider is trying to get. Once the initial images are done, you'll have the dye administered through the intravenous line. The contrast medium could burn a little and some of the reactions mentioned above could happen. Most reactions are nothing to be concerned about. Let the nurse know if you are feeling dizzy, short of breath, or have chest pain. After the contrast medium has been administered, you'll go

back to the X-ray table at regular intervals for additional images. You may have to do this several times and you might be asked to urinate before the final images.

7.5.4 Post-Test

Once the test has been completed, you'll probably be asked by the medical professional to wait a few minutes until the healthcare provider checks to make sure they have all the images they need. As soon as the test is done, the medical professional will remove the intravenous line and you can change back into your clothes.

7.5.5 After the Test

Depending on risk factors, your practitioner might order additional blood tests or exams in the days after an intravenous pyelogram. Be sure to tell the healthcare provider about any difficulty urinating, headaches, or pain after the test.

7.5.6 Results

The images will be interpreted by a radiologist, a healthcare provider specially trained in reading X-rays. The radiologist will send the images and the interpretation back to your healthcare provider, who will share them with you. Intravenous pyelogram interpretation is fairly straightforward and your practitioner (often a urologist) should be able to answer any questions for you.

7.5.7 A Word from Very well

Getting an intravenous pyelogram is very safe and the use of contrast media is widespread throughout medical diagnostics. This test should help guide your healthcare provider as they try to diagnose your condition. It is one tool in the toolbox and might not be able to see everything going on in your kidneys. Understand that

even if this test doesn't tell you the whole story, it's an important part of getting the right answers.

7.6 Extracorporeal Shock Wave Lithotripsy (ESWL)

Extracorporeal Shock Wave Lithotripsy (ESWL) uses sound waves or shock waves to break stones into small fragments that can pass spontaneously. It is performed usually as an outpatient procedure whilst awake or sometimes with sedation. Usually, you can go home immediately after, although it may need to be repeated. Prior to the introduction of extracorporeal shockwave lithotripsy (ESWL) in 1980, the only treatment available for calculi that could not pass through the urinary tract was open surgery. Since then, ESWL has become the preferred tool in the urologist's armamentarium for the treatment of renal stones, proximal stones, and midureteral stones. Compared with open and endoscopic procedures, ESWL is minimally invasive, exposes patients to less anaesthesia, and yields equivalent stone-free rates in appropriately selected patients. Extracorporeal shock wave lithotripsy (ESWL) uses shock waves to break a kidney stone into small pieces that can more easily travel through the urinary tract and pass from the body (National Kidney Foundation Inc, 2022).

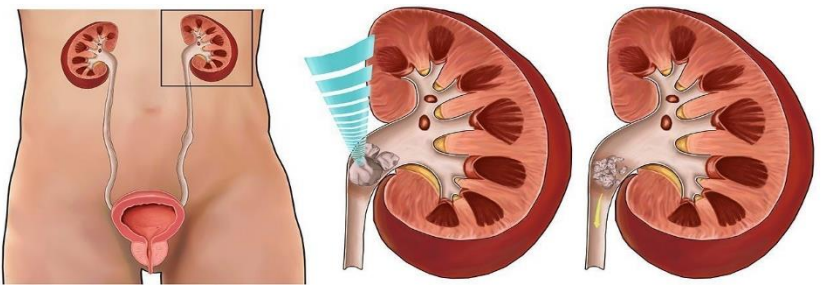


Figure 7.1 Kidney stone inside renal

ESWL may be used on a person who has a kidney stone that is causing pain or blocking the urine flow. Stones that are between 4 mm (0.16 in.) and 2 cm (0.8 in.) in diameter are most likely to be treated with ESWL. ESWL may work best for kidney stones in the kidney or in the part of the ureter close to the kidney. Your surgeon may try to push the stone back into the kidney with a small instrument (ureteroscope) and then use ESWL.

7.6.1 Contra-indications:

- Acute urinary tract infection or urosepsis
- Uncorrected bleeding disorders or coagulopathies
- Pregnancy
- Uncorrected obstruction distal to the stone
- Morbid obesity and orthopaedic or spinal deformities may complicate or prevent proper positioning.
- Renal ectopy or malformations (like horseshoe kidneys and pelvic kidneys)
- Poorly controlled hypertension (due to increased bleeding risk)
- Gastrointestinal disorders: In rare cases, these may be exacerbated after ESWL treatment.
- Renal insufficiency

Shockwaves are generated and then focused onto a point within the body. The shockwaves propagate through the body with negligible dissipation of energy (and therefore damage) owing to the minimal difference in density of the soft tissues. At the stone-fluid interface, the relatively large difference in density, coupled with the concentration of multiple shockwaves in a small area, produces a large dissipation of energy. Via various mechanisms, this energy is then able to overcome the tensile strength of the calculi, leading to fragmentation. Repetition of this process eventually leads to

pulverization of the calculi into small fragments (ideally < 1 mm) that the body can pass spontaneously and painlessly (Khatri, 2022).

- You lie on a water-filled cushion, and the surgeon uses X-rays or ultrasound tests to precisely locate the stone.
- High-energy sound waves pass through your body without injuring it and break the stone into small pieces. These small pieces move through the urinary tract and out of the body more easily than a large stone.
- The process takes about an hour.
- You may receive sedatives or local anaesthesia.
- Your surgeon may use a stent if you have a large stone. A stent is a small, short tube of flexible plastic mesh that holds the ureter open. This helps the small stone pieces to pass without blocking the ureter.

7.6.2 Advantages

There are several advantages of ESWL over other treatments for stones. These include: outpatient procedure that takes 1 hour, reasonably successful, no cutting or invasion of the body at all, low risk of infection from hospital bacteria.

7.6.3 Disadvantages

About 1 in 10 people experience a problem. The main risks are: the treatment does not break the stone, pain as fragments of stone pass down the ureter, blocked urine flow if stone fragments cannot pass down the ureter, urine infection, bleeding around the outside of the kidney.

7.7 Transurethral Resection of the Prostate (TURP)

A transurethral resection of the prostate (TURP) is a surgical procedure done to relieve moderate to severe urinary symptoms caused by an enlarged prostate, a condition known as benign prostatic hyperplasia (BPH). It is used to remove portions of the prostate gland through the penis with the help of an endoscope (small, flexible tube with a light and a lens on the end). A TURP requires no external incision.

TURP is one of the most effective options for treating urinary symptoms caused by BPH. To determine whether TURP or another treatment is the right choice for you, your doctor will consider how severe your symptoms are, what other health problems you have, and the size and shape of your prostate. The prostate gland is about the size of a walnut and surrounds the neck of a man's bladder and urethra—the tube that carries urine from the bladder. It's partly muscular and partly glandular, with ducts opening into the prostatic portion of the urethra. It's made up of three lobes, a center lobe with one lobe on each side.

As part of the male reproductive system, the prostate gland's primary function is to secrete a slightly alkaline fluid that forms part of the seminal fluid (semen), a fluid that carries sperm.

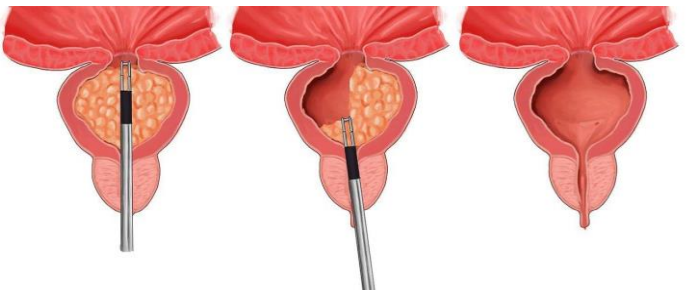


Figure 7.2 TURP

TURP is generally done to relieve symptoms due to prostate enlargement, often due to BPH. When the prostate gland is enlarged, the gland can press against the urethra and interfere with or obstruct the passage of urine out of the body. BPH is a condition in which the prostate gland may become quite enlarged and cause problems with urination. Symptoms may include: problems with getting a urine stream started, having to urinate more frequently at night, having an urgent need to urinate, dribbling after you finish urinating, difficulty emptying bladder, bleeding from prostate, frequent uti (Pruthi, 2022).

These symptoms can create problems such as retaining urine in the bladder, which can contribute to bladder infections or formation of stones in the bladder. BPH can also raise prostate-specific antigen (PSA) levels two to three times higher than the normal level. An increased PSA level doesn't always indicate cancer, but the higher the PSA level, the higher the chance for having cancer. A TURP may be done in men who can't tolerate a radical prostatectomy due to their age or overall health status. Sometimes a TURP is done to treat symptoms only, not to cure the disease. For example, if you're unable to urinate because of cancer, but radical prostatectomy isn't an option for you, you may need a TURP.

You will be given medicine before surgery so you don't feel pain. You may get one of the following (Amwell Surgery, 2022):

- General anaesthesia: you are asleep and pain-free
- Spinal anaesthesia: you are awake, but relaxed and pain-free

A TURP is usually carried out using a device called a resectoscope. A resectoscope is a thin metal tube that contains: light, camera, loop of wire.

The surgeon will insert the resectoscope into your urethra (the tube that carries urine from your bladder to your penis) before guiding it to the site of your prostate with the help of the light and

the camera. An electric current is used to heat the loop of wire, and the heated wire is used to cut away the section of your prostate that is causing your symptoms. After the procedure, a catheter (a thin, flexible tube) is used to pump saline water into the bladder and flush away pieces of prostate that have been removed.

A TURP can take up to an hour to perform, depending on how much of your prostate needs to be removed. Once the procedure has been completed, you will be moved back to your hospital ward so you can recover.

7.7.1 Before the procedure

You will have many visits with your doctor and tests before your surgery. Your visit will include (The John Hopkins, 2022):

- Complete physical exam
- Treating and controlling diabetes, high blood pressure, heart or lung problems, and other conditions

If you are a smoker, you should stop several weeks before the surgery. Your doctor or nurse can give you tips on how to do this.

Always tell your doctor or nurse what drugs, vitamins, and other supplements you are taking, even ones you bought without a prescription. During the weeks before your surgery:

- You may be asked to stop taking medicines that can thin your blood, such as aspirin, ibuprofen (Advil, Motrin), naproxen (Aleve, Naprosyn), vitamin E, clopidogrel (Plavix), warfarin (Coumadin), and others.
- Ask your doctor which drugs you should still take on the day of your surgery.

On the day of your surgery:

- Do not eat or drink anything after midnight the night before your surgery.

- Take the drugs your doctor told you to take with a small sip of water.
- Your doctor or nurse will tell you when to arrive at the hospital

During the procedure

Transurethral resection of the prostate requires a stay in the hospital. Procedures may vary depending on your condition and your doctor's practices.

Generally, a TURP follows this process (The John Hopkins, 2022):

1. You'll be asked to remove any jewelry or other objects that may interfere with the procedure.
2. You'll be asked to remove your clothing and will be given a gown to wear.
3. You'll be asked to empty your bladder prior to the procedure.
4. An intravenous (IV) line will be started in your arm or hand.
5. You'll be positioned on the operating table, lying on your back.
6. The anesthesiologist will continuously monitor your heart rate, blood pressure, breathing, and blood oxygen level during the surgery. Once you're sedated, a breathing tube will be inserted through your throat into your windpipe and you'll be connected to a ventilator, which will breathe for you during the surgery.
7. The surgeon will inspect the urethra and bladder with an endoscope. This is done by passing the scope through the tip of the penis, then into the urethra and bladder. This allows the doctor to examine these areas for any tumors or stones in the bladder.
8. Next, the resectoscope (electrical loop) is passed into the urethra. It cuts out pieces of tissue from the prostate that are

bulging or blocking the urethra. Electricity will be applied through the resectoscope to stop any potential bleeding.

9. The doctor will insert a catheter into the bladder to empty urine.
10. You'll be transferred from the operating table to a bed then taken to the recovery room.

7.7.2 After the procedure

In the hospital

After the procedure, you may be taken to the recovery room to be closely monitored. You'll be connected to monitors that will constantly display your electrocardiogram (ECG or EKG) tracing, blood pressure, other pressure readings, breathing rate, and your oxygen level.

Once your blood pressure, pulse, and breathing are stable and you're alert, you'll be taken to your hospital room. You may receive pain medication as needed. Once you're awake and your condition has stabilized, you may start liquids to drink. Your diet may be gradually advanced to more solid foods as you are able to tolerate them. You will stay in the hospital for 3 days.

After surgery, you will have a small tube, called a Foley catheter, in your bladder to remove urine. The urine will look bloody at first. In most cases, the blood goes away within a few days. Blood can also seep around the catheter. A special solution may be used to flush out the catheter and keep it from getting clogged with blood. The catheter will be removed within 1 to 3 days for most people.

Your health care team will:

- Help you change positions in bed.
- Teach you exercises to keep blood flowing.
- Teach you how to perform coughing and deep breathing techniques. You should do these every 3 to 4 hours.

- Tell you how to care for yourself after your procedure.
  You may need to wear tight stockings and use a breathing device to keep your lungs clear. You may be given medication to relieve bladder spasms (The John Hopkins, 2022).

At Home:

Once you're home, it'll be important to drink lots of fluid. This aids in flushing out any remaining blood or clots from your bladder. You'll be advised to not do any heavy lifting for several weeks after the TURP. This is to prevent any recurrence of bleeding. You may be tender or sore for several days after a TURP. Take a pain reliever for soreness as recommended by your doctor.

Notify your doctor to report any of the following (The John Hopkins, 2022)**:**

- Fever and/or chills
- Redness, swelling, or bleeding or other drainage from the incision site
- Increase in pain around the incision site
- Trouble urinating

TURP is often recommended when prostate enlargement (benign prostatic hyperplasia) causes troublesome symptoms and fails to respond to treatment with medication.

Symptoms that may improve after TURP include:

- problems starting to urinate
- a weak urine flow or stopping and starting
- having to strain to pass urine
- a frequent need to urinate
- waking up frequently during the night to urinate (nocturia)
- a sudden urge to urinate
- being unable to empty your bladder fully

QUIZ : FILL THE BLANK

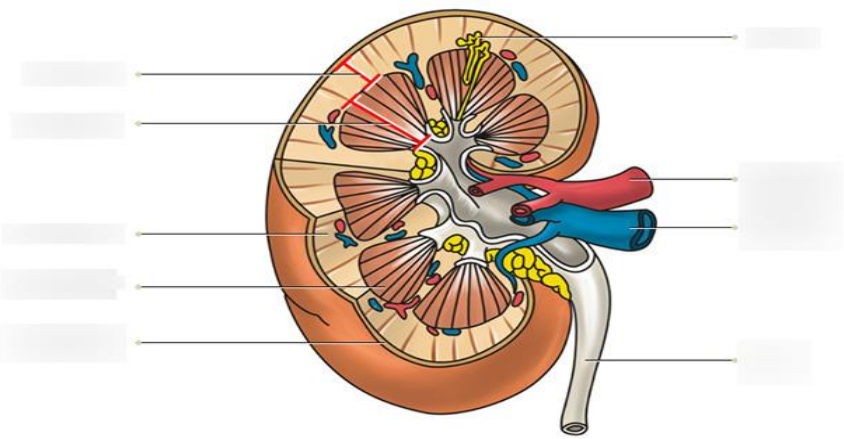
THE GENITOURINARY SYSTEM

FUNCTION: Major organ for_____

SHAPE: _____

COLOR: brownish - red

LOCATION: RETROPERITONEAL AREA? _____angle/flank



FUNCTIONS OF THE KIDNEY

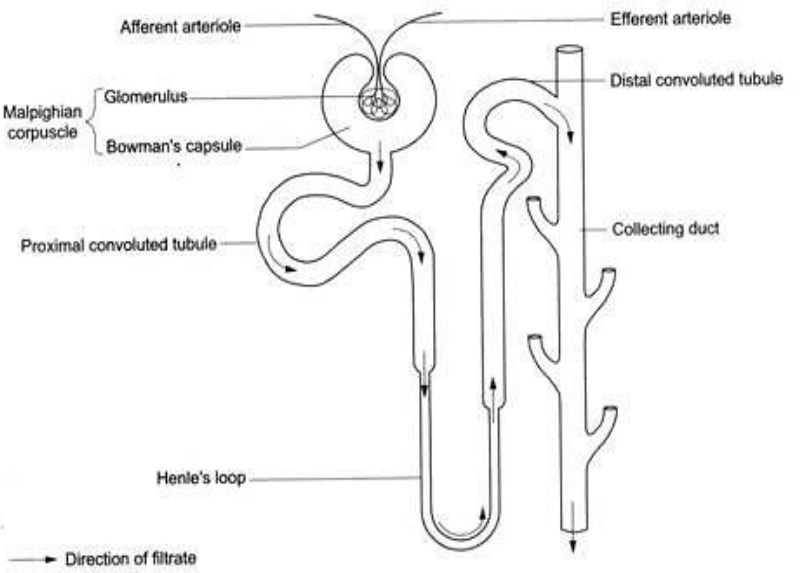
B BP regulation and _____

E Electrolyte balance and _____production

A Acid-base balance

N _____

NEPHRONS - basic functional unit of the Kidney



Different parts of a nephron

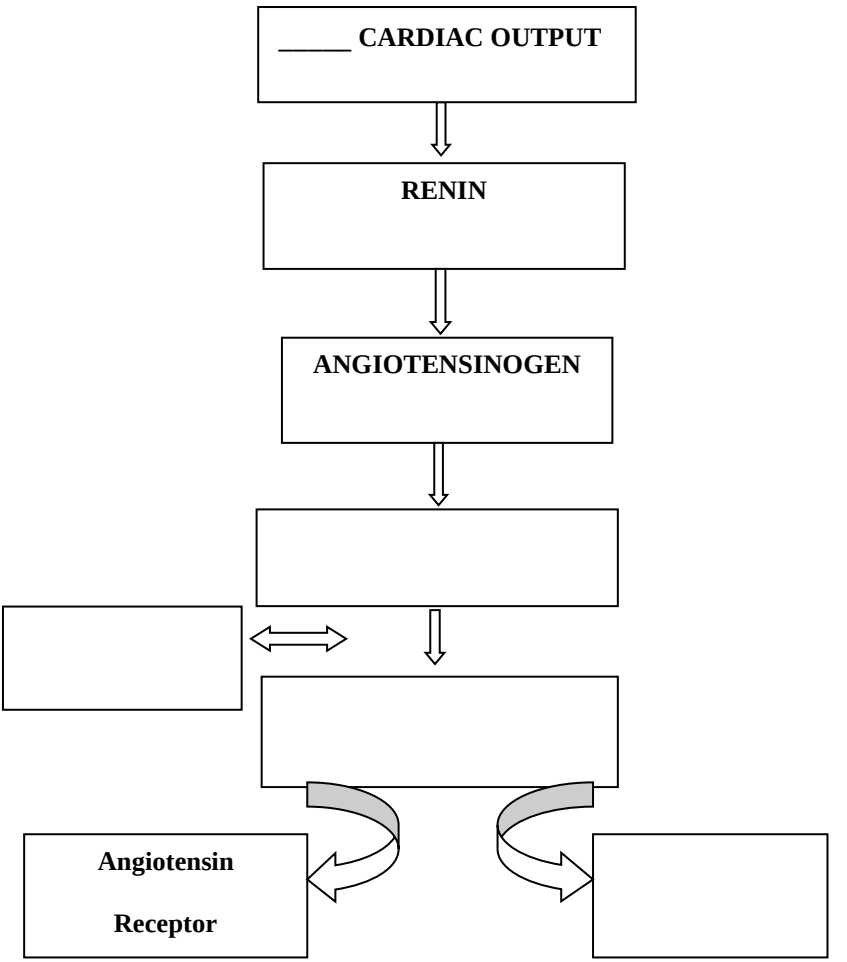
	Function/s
Glomerulus	It is where the initial _____ of blood happens
Proximal convoluted tubule	Tubular _____
Loop of Henle	Controls _____ of the urine
Distal convoluted	Tubular _____
Collecting ducts	_____

ACID - BASE BALANCE

The kidneys will EXCRETE H+ in response to a DECREASING blood pH; they will REABSORB H+ Iin response to an INCREASING blood pH Tto maintain homeostasis.

BP REGULATION:

THE Renin - Angiotensin - Aldosterone System (RAAS)



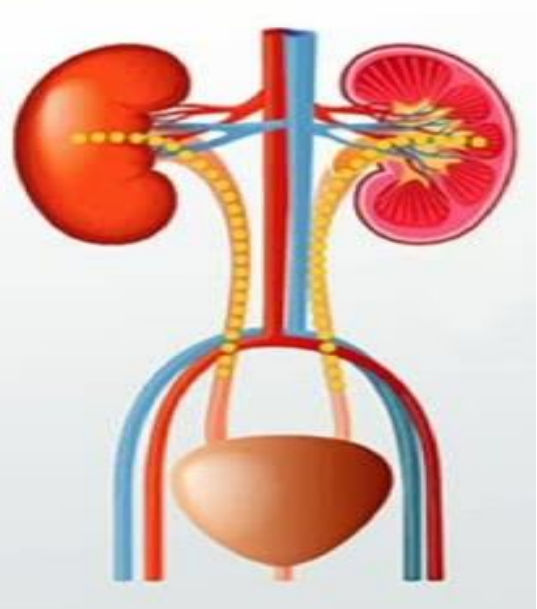
DIAGNOSTIC PROCEDURES:

Intravenous Pyelogram (IVP)	**Renal Angiogram**
Position : Supine Contrast medium: _____ Pre: Assess: Allergy to shellfish NPO _____ Post: Complication:_____	Position: Supine Contrast medium:_____ Inserted at:_____ Anesthesia: _____ Pre: Assess: Allergy to shellfish NPO: Post: Straighten Legs:_____hours Complication: Anaphylact shock, clot fotmation, absence of peripheral pulses

DISORDERS OF THE KIDNEY

RENAL FAILURE

ACUTE	**CHRONIC**
Suddenly, Abruptly Good Prognosis _____ Recovery - within 2 years	_____ Poor Prognosis Irreversible ESRD



Causes of Renal Failure :

Pre-Renal	Intra-Renal	Post-Renal
Poor Perfusion Hypovolemia _____ _ _____ _	Within The Kidneys _____ Nephrotoxic Drugs Infection	Obstruction _____ _____

Activity: Identify the causes of renal failure whether it's PRE-RENAL, INTRA-RENAL OR POST-RENAL

A. BURNS E.ACUTE GLOMERULONEPHRITIS
B. NEOMYCIN F. STREPTOMYCIN
C. BIGUANIDE G. RENAL CALCULI
D. BPH H. HYPOVOLEMIA

ACUTE RENAL FAILURE

OLIGURIC PHASE (_____ cc/day)	
-Fluid retention ● _____ BP ● _____ Diet: ____ Protein ____ K-rich foods ____ salt substitutes ____ Sodium Intake ____ fluid intake	- _____GFR ● ____ BUN ● ____ Crea ● _____ Na ● _____ K

DIURETIC PHASE _____l/day	RECOVERY PHASE
Risk for: _____ Management: _____	Improvement in renal function Normal BUN & Creatinine Normal urine output/hr : 30 cc/hr

Activity: A male client is diagnosed with acute renal failure and manifesting signs and symptoms of oliguric phase. Identify which of the following are associated manifestations during Oliguric Phase	
- INCREASED BUN - DECREASED BUN - DECREASED CREATININE - INCREASED POTASSIUM - DECREASED SODIUM	- AZOTEMIA - EDEMA - HEADACHE - DEHYDRATION

Reduced Renal Reserve Damage: > 75% Compensation: <25% S/sx: ASYMPTOMATIC	Renal Insufficiency Damage: 75% - 90% Compensation: 10-25%	End Stage Renal Disease Damage: 90% - 100% Comensation: 0-10%

	MANIFESTATIONS	**MANAGEMENT**
Blood pressure Bones	_____BP ____Calcium and _____Phosphrus	_____ Phospate Binder: Aluminium Hydroxide (Amphogel)
Erythropoietin Electrolytes	RBC: _____ Increased potassium, Sodium, Phosphorus, Magnesium	_____ _____: DOC for hyperkalemia
Acid-base	Metabolic _____ Kussmaul's breathing	_____
Nitrogenous waste	Azotemia	_____

RENAL FAILURE

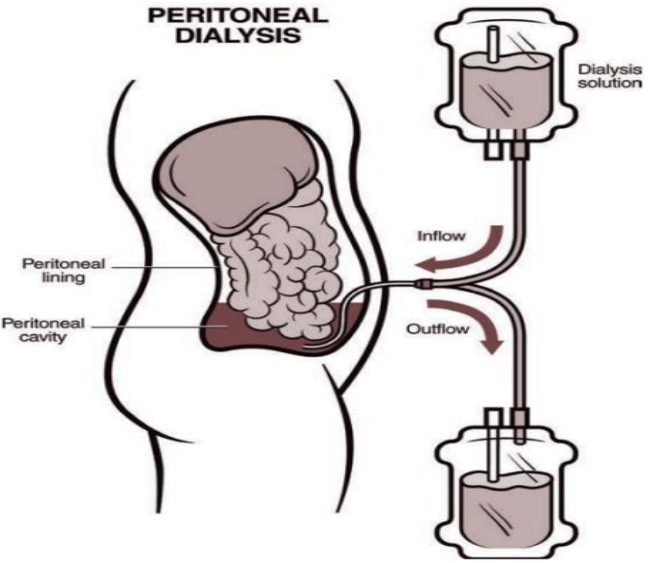
For each statement, identify whether the cause of renal failure is **prerenal, intrarenal, or postrenal**

1. A client is in a motor vehicle accident and ruptures the bladder _____
2. A client overdoses on a nephrotoxic drug _____
3. A client has pregnancy-induced hypertension _____
4. A client is found to have urinary obstruction secondary to uric acid crystals _____
5. A client has systolic heart failure _____
6. A client has anasarca secondary to hypoalbuminemia _____
7. The nurse is examining the specific gravity in the urinalysis of a client in acute renal failure (ARF). typically, the specific gravity result would show that the:
   A. Urine is concentrated, having a specific gravity of 1.045
   B. Urine is dilute, having a specific gravity of 1.000
   C. Specific gravity is equal to that of plasma, 1.010
   D. Urine contains brownish pigmented casts
8. When teaching a client who is prescribed an aminoglycoside, the nurse should be certain to instruct the client:
   a) To drink at least 2-3 L of water per day
   b) To discontinue taking the medication when symptoms subside
   c) To expect changes in the frequency and amount of urination
   d) To hold the medication for one day if the urine becomes concentrated

9. When a client is receiving an aminoglycoside antibiotic, the nurse should monitor which three laboratory values?
   a) _____
   b) _____
   c) _____
10. Which client is at the highest risk for the development of postrenal failure?
   a) A 29 - year-old pregnant female
   b) A 75 - years - old male
   c) A 15 - year - old male with diabetes
   d) A 16 - month - old hospitalized infant
11. Which of the following urine patterns is seen in the maintenance phase of acute renal failure?
   a) Anuria c) Oliguria
   b) Polyuria d) Hypovolemia
12. Which of the following electrolyte imbalances is characteristic of the maintenance phase of acute renal failure?
   a) Hyperkalemia
   b) Hypokalemia
   c) Hypophosphatemia
   d) Hypercalcemia
13. In the client with chronic renal failure, the most common cardiovascular clinical manifestation is:
   a) Edema
   b) Hypertension
   c) Cardiac arrhythmias
   d) Cardiomyopathy
14. Three common problems seen with AV fistulas are:
   a) _____
   b) _____
   c) _____

<table>
<tr><td colspan="2">HEMODIALYSIS</td></tr>
<tr><td colspan="2">DIALYSIS DISEQUILIBRIUM SYNDROME (DDS)</td></tr>
<tr><td colspan="2">Permanent Access - placed _____</td></tr>
<tr><td>AV Fistula
How to check patency:
1.
2.</td><td>AV Graft
Uses an artificial graft known as
_____</td></tr>
<tr><td colspan="2">Temporary Access - placed
_____</td></tr>
<tr><td>Venous Catheter
A. Central-inserted
thru_____vein
B. Peripheral-inserted
thru_____vein
- During the first few days
of dialysis sessions
S/SX: Altered L.O.C
Nausea & vomiting
Seizure
Restlessness
Prevention:
_____</td><td>AV Shunt
Uses 2 silastic ordinary cannula</td></tr>
</table>

Peritoneal Dialysis



Performing the Exchange:

INFUSION - _____ L of dialysate solution (_____ minutes)

_____ - times for the solution to stay in the patients peritoneum (_____ minutes)

TOO MUCH DWELLING: _____

ANTIDOTE: _____

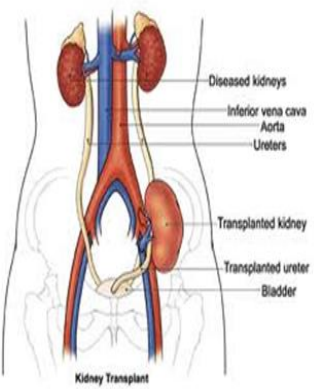
DRAINING - times for the solution to be drained out (_____ minutes)

TOO SLOW DRAINING: _____

ACTIVITY: Identify whether it is Permanent access (hemodialysis), Temporary Access (Hemodialysis) or Peritoneal dialysis.

1. Decrease risk for infection
2. Increase risk for clot formation
3. Readily available
4. Peritoneum serves as an artificial kidney
5. Risk for peritonitis
6. AV Shunt
7. AV graft
8. AV fistula
9. Venous Catheters
10. Involves the use of IV insulin

KIDNEY TRANSPLANT



Cradled at _____

Risk for

Risk for acute

RENAL TRANSPLANTATION

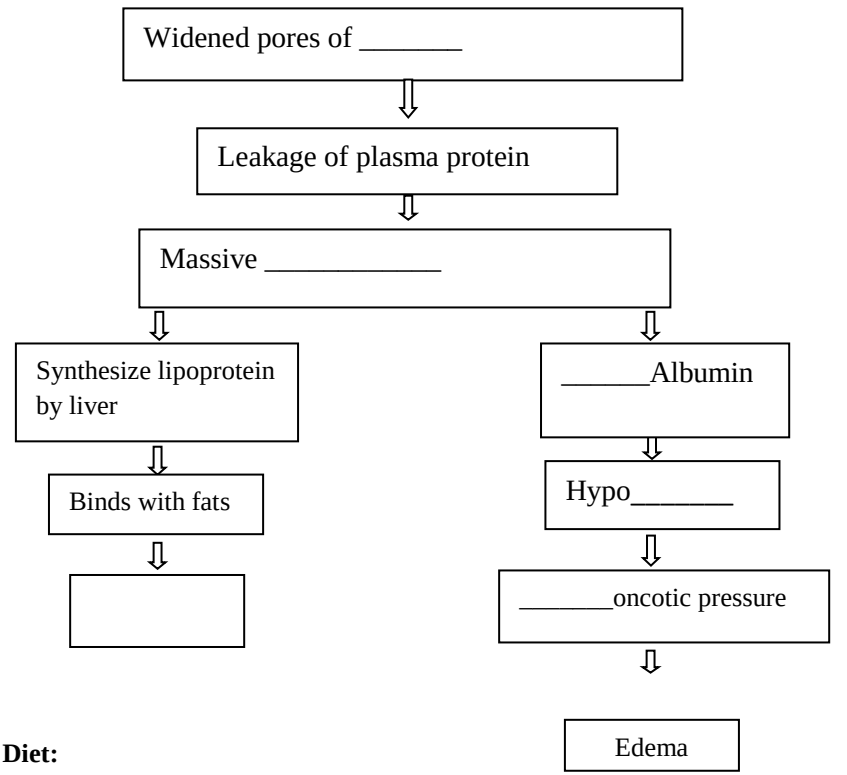
1. A client experiencing an acute rejection of a transplanted kidney would have which of the following physical finding?
   A. Diarrhea
   B. Tenderness at the graft site
   C. Periumbilical discoloration
   D. Increase in urine output
2. Identify two nursing interventions that are appropriate following renal transplantation
   a) _____
   b) _____

3. ACTIVITY: What are the signs of kidney rejection?
G-
R-
A-
F-
T-

Medication to prevent rejection:
Cyclosporine (Sandimmune) - Do not take it with _____ juice (might cause toxicity). _____ and _____ are okay

DISORDERS OF THE NEPHRON

NEPHROTIC Syndrome
Autoimmune Diffuse damage to_____



Diet:
_____ Protein (Lean protein - soya, bean, chicken , fish)
_____ Fats _____ Sodium intake _____ Fluid intake

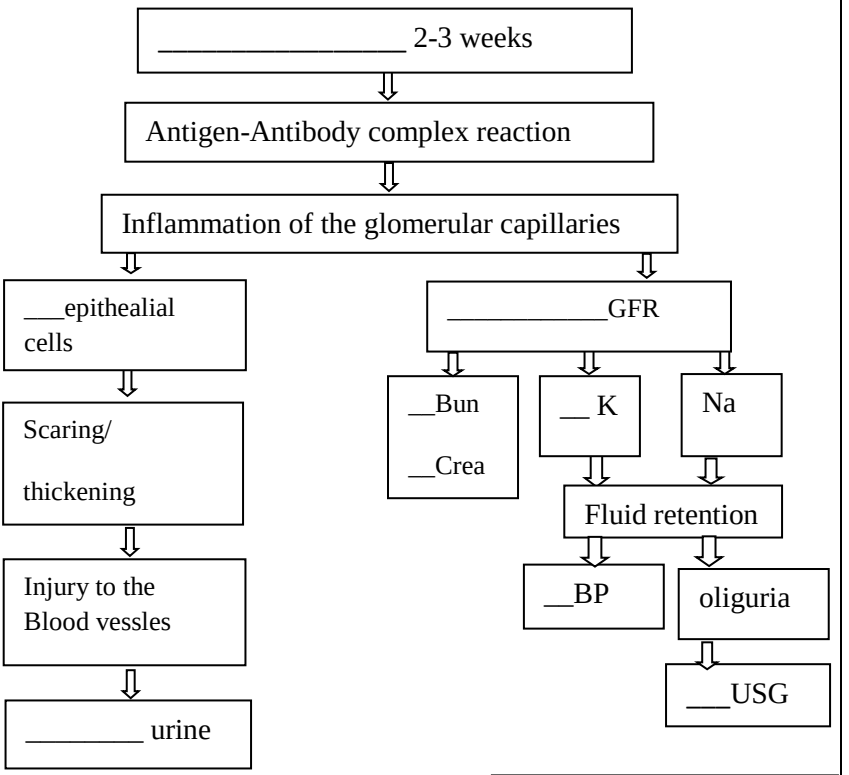
Medications:

- Atorvastatin, Captopril, Diuretics, Corticosteroids, Albumin IV (if indicated by the MD)

DISORDERS OF THE NEPHRON

NEPHRITIC Syndrome

Acute Glomerulonephritis Common Causative Agent:_____ Inflammation of glomeruli due to an antigen-antibody reaction



Diet:___ Protein

___ Sodium

___ Fluid intake

N-o urine/oliguria
E-dema
P-allor
H-ypervolemia
R-eddish brown urine
I-ncrease BUN & Crea
T-enderness (flank area)
I-ncrease specific gravity
S-ore throat

Medications:

Corticosteroid, Antibiotic-Penicillin)

tik- Penicillin, diuretic

Antihypertensives/ACE inhibitors

ACTIVITY: Indicate if it's NEPHROTIC OR NEPHRITIC

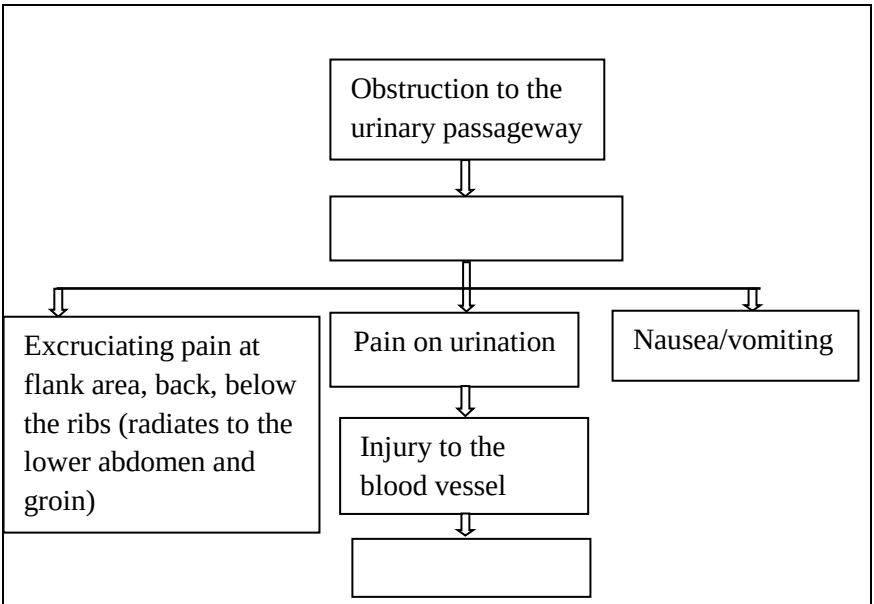
1. GABHS
2. Widened pores of glomerulus
3. Hyperlipidemia
4. Cola-colared urine
5. Hypoalbuminemia
6. Glomerular capillaries inflammation
7. Sorethroat
8. Use Penicillin
9. Decreased Oncotic pressure
10. Frothy urine

RENAL CALCULI

Types of Kidney stones:

Calcium-oxalate stones	**Uric Acid Stones**	**Struvite stones**	**Cystine stones**
Spinach, Rhubarb, Ricebran, Almonds, Wheat berries, Corn grits, Cocoa powder	Anchovies, Lentils, Legumes, Beer, Organ meats, Yeast, Sardines, Salmon, Anchovies	"Infection stones" Associated with UTIs	Rare type Due to excessively high protein diet
Management: _____ DIET Examples: cranberry, corn, cheese, plums, prunes	**Management:** _____ DIET Examples: Milk, green leafy vegetables, and fruits except cranberry, corn, cheese plums, prunes	**Management:** **_____ Protein diet** **____ Sodium diet**	**Management:** **____ Protein diet** **____ Sodium diet**

NEPHROLITHIASIS	**UROLITHIASIS**
Location: _____	Location: _____



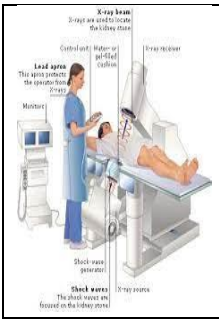
DOC: MeperidineHCL (Demerol)

WOF:

1. Oliguria
2. UTI
3. Hydronephrosis

TREATMENT FOR RENAL CALCULI:_____

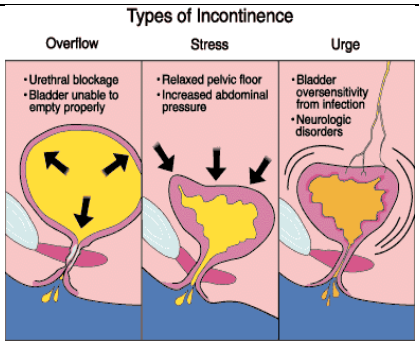
Uses shockwave to break stones in fragments

	POSITION	PRE	POST	COMPLICATION
	_____	NPO ___hours IV sedation	*Bruising	Obstruction hydronephrosis UTI PAIN

WOF:_____(fluid statis sbove the site of obstruction)

Treatment:_____tube

DISORDERS OF THE BLADDER

Types of Urinary Incontine	**Description**	**Identify the Intervention/s**
Figure 2 _____		1. Anticholinergics 2. Bladder Training - done thru timed voiding 3. Pelvic floor exercise - Kegel's exercise 3x/day Benefits: Female:_____ Male:_____
Figure 3 _____		
MIXED STRESS+ URGE		
Figure 1 _____		

FUNCTIONAL	Intact urinary tract but the patient has cognitive impairment	

URINARY TRACT INFECTION (UTI)

PYELONEPHRITIS	**CYCTITIS**
Location: _____	Location: _____

Management:

___ OFI

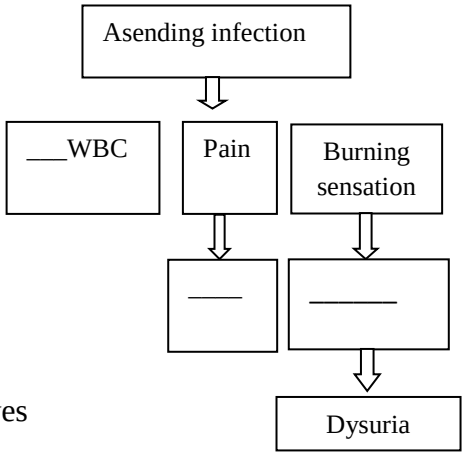
Avoid bladder irritants

Diet: _____

Do: warm sitz bath only

DRUF OF CHOICE:

- Urinary Tract Anti-infectives



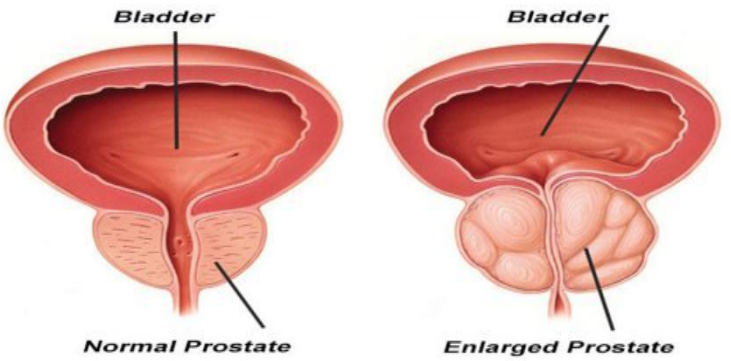
- Methenamine (Hiprex, mandelamine)
- Nalidixic acid (Negram)
- Nitrofurantoin (Macrodantin)
- Sulfisoxazole (Gantrisin)
- TMP - SMZ (Bactrim)

- Urinary Analgesic

- Phenazopyridine (Pyridium)

- Side effect: urine color is _____

DISORDERS OF THE MALE REPRODUCTIVE TRACT
BENIGN PROSTATIC HYPERPLASIA (BPH)

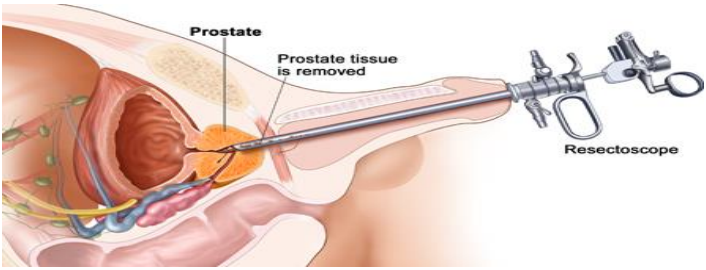


RISK FACTORS:
Male
Age _____ Y.O AND ABOVE
_____ male hormone which affects prostate growth
DIAGNOSTIC TEST:
1. _____

LABORATORY CHECKS:
1. _____ : NORMAL: <4NG/ML
2. Erythrocyte Sedimentation Rate (ESR) Male: normal 0-15 mm/hr

MANAGEMENT:
1. _____ (herbal medication)
2. Finasteride (Proscar)
3. _____ - Antihypertensive drug
WOF:
4. _____ -Urinary Analgesic: to decrease pain upon urination

TREATMENT: Trans-Urethral Resection of the Prostate (TURP)



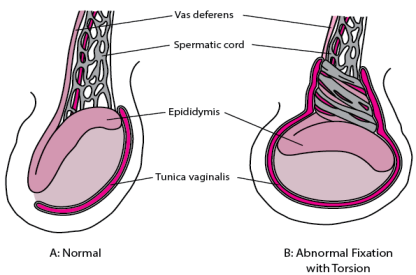
POSITION	PRE	POST	COMPLICATIONS
	NPO:____ ____Anesthesia	CBI-Continous Bladder Irrigation	_____Infection Clot formation-report: _____ spasm

TESTICULAR TORSION

Also known as _____

Common among children _____ years old

Problem: Twisting of the _____



MALE REPRODUCTIVE DRUGS

Sildenafil (Viagra)
Vardenafil (Levitra)
Tadalafil (Cialis)
Take: _____
Onset: _____
Duration: _____
Side effects: _____
Notify: ERECTION> _____HOURS

POINTS TO REMEMBER

STAGES OF BURNS

	STAGE	DEPTH	ASSESSMENT
PARTIAL THICKNESS	1 Superficial	Epidermis with pain	Dry, swelling, red
	2 Deep	Dermis most painful	Red, white, with blister
FULL THICKNESS	3 Full thickness	Subcutaneous and Adipose tissue no pain	Red, white, brown
	4 Deep thickness	Bones and muscles no pain	Black eschar, charred, no edema, dry

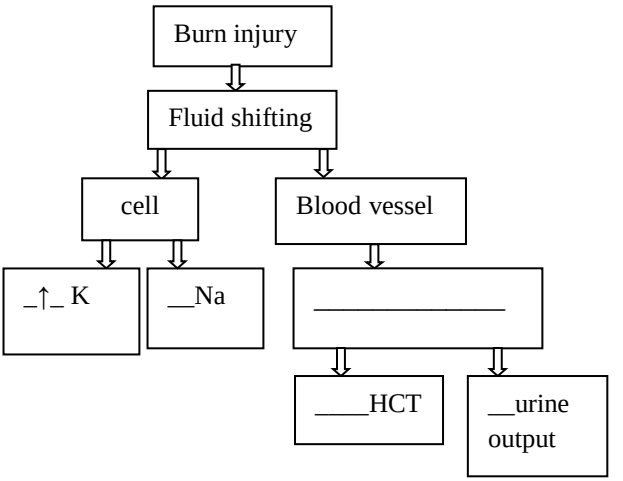
BURN PHASES OF BURNS

EMERGENT PHASE	DIURETIC PHASE	RECOVERY PHASE
"Shock Phase" Vital signs: Dec. Bp and Temp Inc. PR and RR Narrowed pulse pressure Hyponatremia SODIUM DEPLETION DUE TO DESTROYED TISSUES	Fluid shifts back to the blood vessels Hyponatremia INC KIDNEY SODIUM EXCRETION & LOSS OF SODIUM FROM WOUNDS	PRIORITY: Wound care MANAGEMENT: 1. Analgesic: Morphine is given 30 mins prior 2. Prepare: sterile gloves and sponge 3. Culture Sensitivity Test: done to know the appropriate antibiotic to be used 4. Apply Silver sulfadiazine ointment

Hyperkalemia MASSIVE TISSUE NECROSIS & CELL LYSIS Hemoconcentration DUE TO LOSS OF FLUID	Hypokalemia DUE TO DIURESIS Hemodilution	- to stop the growth of bacteria

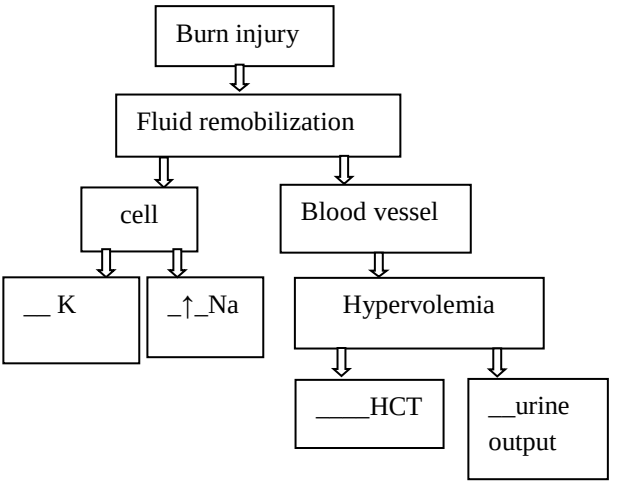
STAGES OF BURNS

EMERGENT PHASE



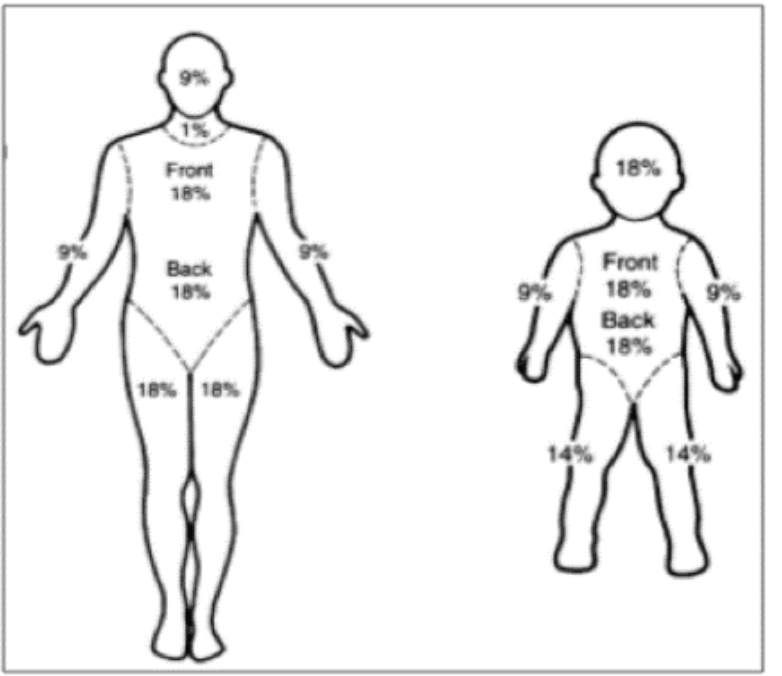
PRIORITY: _____

DIURETIC PHASE



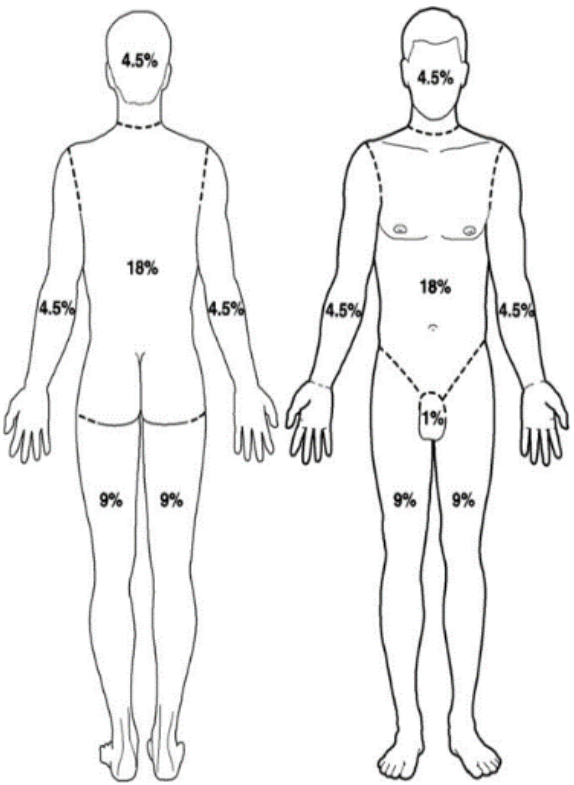
PRIORITY: _____

RULE OF 9'S: TOTAL BODY SURFACE AREA



FLUID RESUSCITATION
BAXTER & PARKLAND METHOD

Total 24 hrs = TBSA X wt (Kg) X 4 mL
First 8 hrs = 1/2 of the total
2nd 16 hrs = 1/2 of the total



___ Entire face and back of the head
___ genitalia
___ circumferential burns of the right arm
___ upper half of the anterior torso
___ circumferential burns of the lower half of both arms
___ anterior half of the head
___ upper half of posterior torso

REFERENCES

Aboumarzouk, O. M., Kata, S. G., Keeley, F. X., McClinton, S., & Nabi, G. (2012). Extracorporeal shock wave lithotripsy (ESWL) versus ureteroscopic management for ureteric calculi. *The Cochrane Database of Systematic Reviews*, *5*.

Adler, S. M., & Wartofsky, L. (2007). The nonthyroidal illness syndrome. *Endocrinology and Metabolism Clinics of North America*, *36*(3), 657–672.

Almeras, C., & Argilés, À. (2009). The general picture of uremia. *Seminars in Dialysis*, *22*(4), 329–333.

Amer, T., Ahmed, K., Bultitude, M., Khan, S., Kumar, P., De Rosa, A., Khan, M. S., & Hegarty, N. (2012). Standard versus tubeless percutaneous nephrolithotomy: a systematic review. *Urologia Internationalis*, *88*(4), 373–382.

Amwell Surgery. (2022). *Transurethral resection of the prostate (TURP)*. Amwell Surgery. https://amwellsurgery.co.uk/conditions/transurethral-resection-of-the-prostate-turp/

Bachmann, A., & Rosette, J. (2012). *Benign Prostatic Hyperplasia and Lower Urinary Tract Symptoms in Men*. Oxford University Press.

Bagga, H. S., Chi, T., Miller, J., & Stoller, M. L. (2013). New insights into the pathogenesis of renal calculi. *The Urologic Clinics of North America*, *40*(1), 1–12.

Bakris, G. L. (2012). Lipid disorders in uremia and dialysis. *Contributions to Nephrology*, *178*, 100–105.

Bellomo, R., Kellum, J. A., & Ronco, C. (2012). Acute kidney injury. *Lancet (London, England)*, *380*(9843), 756–766.

Bellomo, R., Ronco, C., Kellum, J. A., Mehta, R. L., & Palevsky, P. (2004). Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Critical Care (London, England)*, *8*(4).

Bhandari, S. (2011). Risk factors and metabolic mechanisms in the pathogenesis of uraemic cardiac disease. *Frontiers in Bioscience (Landmark Edition)*, *16*(4), 1364–1387.

Bonventre, J. V., & Yang, L. (2011). Cellular pathophysiology of ischemic acute kidney injury. *The Journal of Clinical Investigation*, *121*(11), 4210–4221.

Bouglé, A., & Duranteau, J. (2011). Pathophysiology of sepsis-induced acute kidney injury: the role of global renal blood flow and renal vascular resistance. *Contributions to Nephrology*, *174*, 89–97.

Briet, M., & Burns, K. D. (2012). Chronic kidney disease and vascular remodelling: molecular mechanisms and clinical implications. *Clinical Science (London, England : 1979)*, *123*(7), 399–416.

Chandhoke, P. S. (2007). Evaluation of the recurrent stone former. *The Urologic Clinics of North America*, *34*(3), 315–322.

Chauveau, P., & Aparicio, M. (2011). Benefits in nutritional interventions in patients with CKD stage 3-4. *Journal of Renal Nutrition : The Official Journal of the Council on Renal Nutrition of the National Kidney Foundation*, *21*(1), 20–22.

Chughtai, B., Lee, R., Te, A., & Kaplan, S. (2011). Inflammation and benign prostatic hyperplasia: clinical implications. *Current Urology Reports*, *12*(4), 274–277. https://doi.org/10.1007/S11934-011-0191-3

Clarkson, M., Friedewald, J., Eustace, J., & Rabb, H. (2007). *Acute kidney injury* (8th editio). Saunders Elsevier.

Coca, S. G., Singanamala, S., & Parikh, C. R. (2012). Chronic kidney disease after acute kidney injury: a systematic review and meta-analysis. *Kidney International*, *81*(5), 442–448. https://pubmed.ncbi.nlm.nih.gov/22113526/

Coe, F. L., Evan, A., & Worcester, E. (2011). Pathophysiology-based treatment of idiopathic calcium kidney stones. *Clinical Journal of the American Society of Nephrology : CJASN*, *6*(8), 2083–2092.

Cooperberg, M., Presti, J., Shinohara, K., & Carroll, P. (2012). Neoplasms of the prostate gland. In *Smith and Tanagho's general urology* (18th editi). McGraw-Hill Lange.

Cosgrove, D. (2012). Glomerular pathology in Alport syndrome: a molecular perspective. *Pediatric Nephrology (Berlin, Germany)*, *27*(6), 885–890.

Cruz, D. N., Bagshaw, S. M., Ronco, C., & Ricci, Z. (2010). Acute kidney injury: classification and staging. *Contributions to Nephrology*, *164*, 24–32.

Curhan, G. C. (2007). Epidemiology of Stone Disease. *The Urologic Clinics of North America*, *34*(3), 287.

De Seigneux, S., & Martin, P. (2009). Management of patients with nephrotic syndrome. *Swiss Med Wkly*, *139*, 416–422.

Evan, A. P. (2010). Physiopathology and etiology of stone formation in the kidney and the urinary tract. *Pediatric Nephrology (Berlin, Germany)*, *25*(5), 831–841.

Fabbian, F., Casetta, I., Giorgi, A. De, Pala, M., Tiseo, R., Portaluppi, F., & Manfredini, R. (2012). Stroke and renal dysfunction: are we always conscious of this relationship? *Clinical and Applied Thrombosis/Hemostasis : Official Journal of the International Academy of Clinical and Applied Thrombosis/Hemostasis*, *18*(3), 305–311.

Fassett, R. G., Venuthurupalli, S. K., Gobe, G. C., Coombes, J. S., Cooper, M. A., & Hoy, W. E. (2011). Biomarkers in chronic kidney disease: a review. *Kidney International*, *80*(8), 806–821.

Ferguson, M. A., & Waikar, S. S. (2012). Established and emerging markers of kidney function. *Clinical Chemistry*, *58*(4), 680–689.

Fink, H. A., Ishani, A., Taylor, B. C., Greer, N. L., Roderick MacDonald, D. R., Sadiq, S., Srilakshmi Lankireddy, R. L. K., & Wilt, T. J. (2012). *Chronic kidney disease stages 1-3: screening, monitoring, and treatment*. Agency for Healthcare Research and Quality.

Fleming, G. M. (2011). Renal replacement therapy review: past, present and future. *Organogenesis*, *7*(1), 2–12.

Fouque, D., Pelletier, S., Mafra, D., & Chauveau, P. (2011). Nutrition and chronic kidney disease. *Kidney International*, *80*(4), 348–357.

Galle, P., & Labejof, L. (2011). In nephrotic syndromes podocytes synthesize and excrete proteins into the tubular fluid: an electron and ion microscopic study. *Comptes Rendus Biologies*, *334*(10), 713–719.

Garg, R., & Williams, M. E. (2013). Diabetes management in the kidney patient. *The Medical Clinics of North America*, *97*(1), 135–156.

Gorriz, J. L., & Martinez-Castelao, A. (2012). Proteinuria: detection and role in native renal disease progression. *Transplantation Reviews (Orlando, Fla.)*, *26*(1), 3–13.

Graham, A., Luber, S., & Wolfson, A. B. (2011). Urolithiasis in the emergency department. *Emergency Medicine Clinics of North America*, *29*(3), 519–538.

Grgic, I., Campanholle, G., Bijol, V., Wang, C., Sabbisetti, V. S., Ichimura, T., Humphreys, B. D., & Bonventre, J. V. (2012). Targeted proximal tubule injury triggers interstitial fibrosis and glomerulosclerosis. *Kidney International*, *82*(2), 172–183.

Hewitt, J., Uniacke, M., Hansi, N. K., Venkat-Raman, G., & Mccarthy, K. (2012). Sodium bicarbonate supplements for treating acute kidney injury. *The Cochrane Database of Systematic Reviews*, *2012*(6).

Himmelfarb, J., & Ikizler, T. A. (2010). Hemodialysis. *The New England Journal of Medicine*, *363*(19), 1833–1845.

Honore, P. M., Jacobs, R., Joannes-Boyau, O., De Regt, J., Boer, W., De Waele, E., Collin, V., & Spapen, H. D. (2011). Septic AKI in ICU patients. diagnosis, pathophysiology, and treatment type, dosing, and timing: a comprehensive review of recent and future developments. *Annals of Intensive Care*, *1*(1).

Iglesias, P., Carrero, J. J., & Díez, J. J. (2012). Gonadal dysfunction in men with chronic kidney disease: clinical features, prognostic implications and therapeutic options. *Journal of Nephrology*, *25*(1), 31–42.

Iglesias, P., & Díez, J. J. (2009). Thyroid dysfunction and kidney disease. *European Journal of Endocrinology*, *160*(4), 503–515.

Ikee, R., Hamasaki, Y., Oka, M., Maesato, K., Mano, T., Moriya, H., Ohtake, T., & Kobayashi, S. (2008). Glucose metabolism, insulin resistance, and renal pathology in non-diabetic chronic kidney disease. *Nephron. Clinical Practice*, *108*(2).

Jia, T., Carrero, J. J., Lindholm, B., & Stenvinkel, P. (2012). The complex role of adiponectin in chronic kidney disease. *Biochimie*, *94*(10), 2150–2156.

Joannidis, M., & Forni, L. G. (2011). Clinical review: timing of renal replacement therapy. *Critical Care (London, England)*, *15*(3).

Kapoor, A. (2012). Benign prostatic hyperplasia (BPH) management in the primary care setting. *Can J Urol*, *19*(1).

Kaw, D., & Malhotra, D. (2006). Platelet dysfunction and end-stage renal disease. *Seminars in Dialysis*, *19*(4), 317–322.

KD, N., O, E., M, G., J, Y., SY, H., S, S., GP, H., L, V., ST, R., M, N., & ND, V. (2011). Chronic inflammatory disorders and accelerated atherosclerosis: chronic kidney disease. *Current Pharmaceutical Design*, *17*(1), 17–20.

Kerlin, B. A., Ayoob, R., & Smoyer, W. E. (2012). Epidemiology and pathophysiology of nephrotic syndrome-associated thromboembolic disease. *Clinical Journal of the American Society of Nephrology : CJASN*, *7*(3), 513–520.

Khanna, R. (2011). Clinical Presentation & Management of Glomerular Diseases: Hematuria, Nephritic & Nephrotic Syndrome. *Missouri Medicine*, *108*(1), 33.

Khatri, M. (2022). *When Do I Need Surgery for a Kidney Stone?* WebMD. https://www.webmd.com/kidney-stones/surgery-for-kidney-stone

Kopple, J. D. (2001). National kidney foundation K/DOQI clinical practice guidelines for nutrition in chronic renal failure. *American Journal of Kidney Diseases : The Official Journal of the National Kidney Foundation*, *37*(1 Suppl 2).

Kovesdy, C. P. (2012). Significance of hypo- and hypernatremia in chronic kidney disease. *Nephrology, Dialysis, Transplantation : Official Publication of the European Dialysis and Transplant Association - European Renal Association*, *27*(3), 891–898.

Kraut, J. A., & Madias, N. E. (2011). Consequences and therapy of the metabolic acidosis of chronic kidney disease. *Pediatric Nephrology (Berlin, Germany)*, *26*(1), 19–28.

Krishnan, A. V., & Kiernan, M. C. (2007). Uremic neuropathy: clinical features and new pathophysiological insights. *Muscle & Nerve*, *35*(3), 273–290.

Lee, D. W., Faubel, S., & Edelstein, C. L. (2011). Cytokines in acute kidney injury (AKI). *Clinical Nephrology*, *76*(3), 165–173.

Lehnhardt, A., & Kemper, M. J. (2011). Pathogenesis, diagnosis and management of hyperkalemia. *Pediatric Nephrology (Berlin, Germany)*, *26*(3), 377–384.

Libetta, C., Sepe, V., Esposito, P., Galli, F., & Dal Canton, A. (2011). Oxidative stress and inflammation: Implications in uremia and hemodialysis. *Clinical Biochemistry*, *44*(14–15), 1189–1198.

Lingeman, J., & Lifshitz, D. (2002). Surgical management of urinary lithiasis. In *Campbell's urology*. Elsevier Saunders.

Locatelli, F., & Del Vecchio, L. (2011). New erythropoiesis-stimulating agents and new iron formulations. *Contributions to Nephrology*, *171*, 255–260.

Lombel, R. M., Hodson, E. M., & Gipson, D. S. (2013). Treatment of steroid-resistant nephrotic syndrome in children: new guidelines from KDIGO. *Pediatric Nephrology (Berlin, Germany)*, *28*(3), 409–414.

Mandeville, J. A., Gnessin, E., & Lingeman, J. E. (2011). Imaging evaluation in the patient with renal stone disease. *Seminars in Nephrology*, *31*(3), 254–258.

Manenti, L., Tansinda, P., & Vaglio, A. (2009). Uraemic pruritus: clinical characteristics, pathophysiology and treatment. *Drugs*, *69*(3), 251–263.

McCance, Huether, Brashers, & Rote. (2014). *Pathophysiolopgy : The Biologic for Disease in Adults and Children* (7th Editio). Mosby Elsevier.

McCullough, P. A., Steigerwalt, S., Tolia, K., Chen, S. C., Li, S., Norris, K. C., & Whaley-Connell, A. (2011). Cardiovascular disease in chronic kidney disease: data from the Kidney Early Evaluation Program (KEEP). *Current Diabetes Reports*, *11*(1), 47–55.

Mejía, N., Roman-García, P., Miar, A. B., Tavira, B., & Cannata-Andía, J. B. (2011). Chronic kidney disease--mineral and bone disorder: a complex scenario. *Nefrologia : Publicacion Oficial de La Sociedad Espanola Nefrologia*, *31*(5), 514–519.

National Kidney Foundation Inc. (2022). *Kidney Stone Treatment: Shock Wave Lithotripsy*. National Kidney Foundation. https://www.kidney.org/atoz/content/kidneystones_shockwave

Nevis, I. F., Reitsma, A., Dominic, A., McDonald, S., Thabane, L., Akl, E. A., Hladunewich, M., Akbari, A., Joseph, G., Sia, W., Iansavichus, A. V., & Garg, A. X. (2011). Pregnancy outcomes in women with chronic kidney disease: a systematic review. *Clinical Journal of the American Society of Nephrology : CJASN*, *6*(11), 2587–2598.

Nicholas, S. B., Vaziri, N. D., & Norris, K. C. (2013). What should be the blood pressure target for patients with chronic kidney disease? *Current Opinion in Cardiology*, *28*(4), 439–445.

Nicholson, T. M., & Ricke, W. A. (2011). Androgens and estrogens in benign prostatic hyperplasia: past, present and future. *Differentiation; Research in Biological Diversity*, *82*(4–5), 184–199. https://doi.org/10.1016/J.DIFF.2011.04.006

O'Toole, S. M., Fan, S. L., Yaqoob, M. M., & Chowdhury, T. A. (2012). Managing diabetes in dialysis patients. *Postgraduate Medical Journal*, *88*(1037), 160–166.

Odutayo, A., & Cherney, D. (2012). Cystatin C and acute changes in glomerular filtration rate. *Clinical Nephrology*, *78*(1), 64–75.

Ortiz-Alvarado, O., Miyaoka, R., Kriedberg, C., Moeding, A., Stessman, M., Anderson, J. K., & Monga, M. (2011). Impact of dietary counseling on urinary stone risk parameters in recurrent stone formers. *Journal of Endourology*, *25*(3), 535–540.

Ortiz, A., Justo, P., Sanz, A., Lorz, C., & Egido, J. (2003). Targeting apoptosis in acute tubular injury. *Biochemical Pharmacology*, *66*(8), 1589–1594.

Ott, S. M. (2012). Bone disease in CKD. *Current Opinion in Nephrology and Hypertension*, *21*(4), 376–381.

Palevsky, P. M. (2013). Renal replacement therapy in acute kidney injury. *Advances in Chronic Kidney Disease*, *20*(1), 76–84.

Patton, K., & Thibodeau, G. (2013). *Anatomy & physiology* (8th editio). Mosby.

Platz, E. A., Joshu, C. E., Mondul, A. M., Peskoe, S. B., Willett, W. C., & Giovannucci, E. (2012). Incidence and progression of lower urinary tract symptoms in a large prospective cohort of United States men. *The Journal of Urology*, *188*(2), 496–501. https://doi.org/10.1016/J.JURO.2012.03.125

Port, M. . (2011). *Essentials of Pathophysiology Concepts of Altered health States* (4th Editio). Lippincott Williams&Wilkins.

Prabhu, M. V., Nayak, A., Sridhar, G., Subhramanyam, S. V., & Nayak, K. S. (2012). Maximizing the erythropoietin response: iron strategies. *Contributions to Nephrology*, *178*, 95–99.

Pruthi, S. (2022). *Transurethral resection of the prostate (TURP)*. Mayo Clinic. https://www.mayoclinic.org/tests-procedures/turp/about/pac-20384880

Pyram, R., Kansara, A., Banerji, M. A., & Loney-Hutchinson, L. (2012). Chronic kidney disease and diabetes. *Maturitas*, *71*(2), 94–103.

Rosołowska-Huszcz, D., Kozłowska, L., & Rydzewski, A. (2005). Influence of low protein diet on nonthyroidal illness syndrome in chronic renal failure. *Endocrine*, *27*(3), 283–288.

Rule, A. D., Krambeck, A. E., & Lieske, J. C. (2011). Chronic kidney disease in kidney stone formers. *Clinical Journal of the American Society of Nephrology : CJASN*, *6*(8), 2069–2075.

Rule, A. D., Roger, V. L., Melton, L. J., Bergstralh, E. J., Li, X., Peyser, P. A., Krambeck, A. E., & Lieske, J. C. (2010). Kidney Stones Associate with Increased Risk for Myocardial Infarction. *Journal of the American Society of Nephrology : JASN*, *21*(10), 1641.

Rüster, C., & Wolf, G. (2011). Angiotensin II as a morphogenic cytokine stimulating renal fibrogenesis. *Journal of the American Society of Nephrology : JASN*, *22*(7), 1189–1199.

Saeed, F., Agrawal, N., Greenberg, E., & Holley, J. L. (2011). Lower gastrointestinal bleeding in chronic hemodialysis patients. *International Journal of Nephrology*, *2011*, 1–8.

Sakhaee, K., Maalouf, N. M., & Sinnott, B. (2012). Clinical review. Kidney stones 2012: pathogenesis, diagnosis, and management. *The Journal of Clinical Endocrinology and Metabolism*, *97*(6), 1847–1860.

Sampson, N., Madersbacher, S., & Berger, P. (2008). [Pathophysiology and therapy of benign prostatic hyperplasia]. *Wiener Klinische Wochenschrift*, *120*(13–14), 390–401. https://doi.org/10.1007/S00508-008-0986-5

Sas, D. J. (2011). An update on the changing epidemiology and metabolic risk factors in pediatric kidney stone disease. *Clinical Journal of the American Society of Nephrology : CJASN*, *6*(8), 2062–2068.

Sharfuddin, A., Weisbord, S., & Palevsky, P. (2012). *Acute Kidney Injury* (9th editio). Saunders Elsevier.

Siddall, E. C., & Radhakrishnan, J. (2012). The pathophysiology of edema formation in the nephrotic syndrome. *Kidney International*, *82*(6), 635–642.

Sorensen, M. V., Matos, J. E., Praetorius, H. A., & Leipziger, J. (2010). Colonic potassium handling. *Pflugers Archiv : European Journal of Physiology*, *459*(5), 645–656.

Svenningsen, P., Skøtt, O., & Jensen, B. L. (2012). Proteinuric diseases with sodium retention: Is plasmin the link? *Clinical and Experimental Pharmacology & Physiology*, *39*(1), 117–124.

The John Hopkins. (2022). *Transurethral Resection of the Prostate (TURP)*. John Hopkins Medicine. https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/transurethral-resection-of-the-prostate-turp

Thorp, M. L., Smith, D. H., Johnson, E. S., Vupputuri, S., Weiss, J. W., Petrik, A. F., Yang, X., Levey, A. S., Wasse, H., Muoneke, R., & Snyder, S. R. (2012). Proteinuria among patients with chronic kidney disease: a performance measure for improving patient outcomes. *Joint Commission Journal on Quality and Patient Safety*, *38*(6), 277–282.

Timms, B. G., & Hofkamp, L. E. (2011). Prostate development and growth in benign prostatic hyperplasia. *Differentiation; Research in Biological Diversity*, *82*(4–5), 173–183. https://doi.org/10.1016/J.DIFF.2011.08.002

Tiselius, H. G. (2011). A hypothesis of calcium stone formation: an interpretation of stone research during the past decades. *Urological Research*, *39*(4), 231–243.

Ulinsky, T., & Aoun, B. (2012). New treatment strategies in idiopathic nephrotic syndrome. *Minerva Pediatr*, *64*(2).

Van Buren, P. N., & Inrig, J. K. (2012). Hypertension and hemodialysis: pathophysiology and outcomes in adult and pediatric populations. *Pediatric Nephrology (Berlin, Germany)*, *27*(3), 339.

Vaziri, N. D., Pahl, M. V., Crum, A., & Norris, K. (2012). Effect of uremia on structure and function of immune system. *Journal of Renal Nutrition : The Official Journal of the Council on Renal Nutrition of the National Kidney Foundation*, *22*(1), 149–156.

Viswanathan, G., & Upadhyay, A. (2011). Assessment of proteinuria. *Advances in Chronic Kidney Disease*, *18*(4), 243–248.

Wagner, C., & Mohebbi, N. (2010). Urinary pH and stone formation. *J Nephrol*, *23*(16).

Yang, L., Humphreys, B. D., & Bonventre, J. V. (2011). Pathophysiology of acute kidney injury to chronic kidney disease: maladaptive repair. *Contributions to Nephrology*, *174*, 149–155.

Zarjou, A., & Agarwal, A. (2011). Sepsis and acute kidney injury. *Journal of the American Society of Nephrology : JASN*, *22*(6), 999–1006.

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