

Nephrology and Kidney

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Abstract: Nephrology is a major for the study and medicine of kidney. A physician whose expert is in nephrology is a nephrologist or renal physician. Nephrology does the diagnosis and treatment of kidney diseases, which includes electrolyte disturbances, hypertension, dialysis and renal transplant patients, etc. Nephrology deals many contents, such as kidney systemic disorders, systemic vasculitides, autoimmune diseases, lupus, congenital defection, genetic problem, polycystic kidney disease, acute renal failure, chronic kidney disease, hematuria, proteinuria, kidney stones, hypertension, and disorders of acid/base or electrolytes, cancer-related kidney diseases.

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The kidneys are bean-shaped organs that remove excess waste products of metabolism from body through blood flow. They are essential in the urinary system and also serve homeostatic functions such as the regulation of electrolytes, maintenance of acid–base balance, and regulation of blood pressure. The kidney works in the animal body as a natural filter of the blood to remove water soluble wastes to the bladder. In producing urine, the kidneys excrete wastes such as urea and ammonium, and they are also responsible for the reabsorption of water, glucose, and amino acids. The kidneys also produce hormones including calcitriol, erythropoietin and the enzyme renin, etc. If the kidney completely stops work, the animal will die in a few days.

Located at the rear of the abdominal cavity in the retroperitoneal space, the kidneys receive blood from the paired renal arteries, and drain into the paired renal veins. Normally one animal has two kidneys and each kidney excretes urine into a ureter and flows into the bladder independently.

Nephrology is a major for the study and medicine of kidney. A medical physician whose expert is in nephrology is a nephrologist or renal physician. Normally in most hospitals nephrology belongs to the internal medicine.

Nephrology does the diagnosis and treatment of kidney diseases including electrolyte disturbances, hypertension, dialysis and renal transplant patients, etc. Nephrology plays important roles in human health and it deals many contents such as kidney systemic disorders,

systemic vasculitides, autoimmune diseases, lupus, congenital defection, genetic problem, polycystic kidney disease, acute renal failure, chronic kidney disease, hematuria, proteinuria, kidney stones, hypertension, disorders of acid/base or electrolytes and cancer-related kidney diseases (Onconeurology), etc.

Like other medicine works, normally the nephrology diagnosis includes regarding family history, general medical history, age, feeling, living condition, diet, medication use, drug use and job, etc. Examination typically includes blood pressure, assessment of volume state, skin, joints, abdomen and flank, normal urine examination (urinalysis), blood in the urine (haematuria), protein in the urine (proteinuria), pus cells in the urine (pyuria) or cancer cells in the urine, etc. A 24-hour urine collection can be used to quantify daily protein loss, urine output, creatinine clearance or electrolyte handling by the renal tubules. Basic blood tests will check the hemoglobin, platelets, sodium, potassium, chloride, bicarbonate, urea, creatinine, calcium, magnesium and phosphate in the blood, infections (hepatitis B, hepatitis C), autoimmune conditions (systemic lupus erythematosus, ANCA vasculitis), paraproteinemias (amyloidosis, multiple myeloma), metabolic diseases (diabetes, cystinosis), biopsy of kidney (renal biopsy) and pathology, etc. The serum creatinine concentration can be used to estimate the function of the kidney [creatinine clearance or estimated glomerular filtration rate (GFR)]. Structural abnormalities of the kidneys are checked with

imaging tests, such as medical ultrasonography/ultrasound, computed axial tomography (CT), scintigraphy (nuclear medicine), angiography or magnetic resonance imaging (MRI).

The kidney is involved in whole-body homeostasis, regulating acid-base balance, electrolyte concentrations, extracellular fluid volume and blood pressure, etc. The kidney accomplishes these homeostatic functions both independently and in concert with other organs, particularly those of the endocrine system. Various endocrine hormones coordinate these endocrine functions which include renin, angiotensin II, aldosterone, antidiuretic hormone and atrial natriuretic peptide, etc. Kidney's most functions are accomplished by filtration, reabsorption and secretion, etc, and the functions take place in the nephron. Filtration, which takes place at the renal corpuscle, is the process by which cells and large proteins are filtered from the blood to make an ultrafiltrate that eventually becomes urine. The kidney generates 180 liters of filtrate a day, while reabsorbing a large percentage, allowing for the generation of only approximately 2 liters of urine. Reabsorption is the transport of molecules from this ultrafiltrate and into the blood. Secretion is the reverse process, in which molecules are transported in the opposite direction, from the blood into the urine. If the kidney functions of filtration, reabsorption and secretion fail, the animal will be poisoned by the waste products and takes disease.

Treatments in nephrology can include medications, blood products, surgical interventions (urology, vascular or surgical procedures), renal replacement therapy (dialysis or kidney transplantation), plasma exchange and stem cell transplantation, etc. Chronic kidney disease is typically managed with treatment of causative conditions, avoidance of substances toxic to the kidneys, antihypertensives, diet and weight modification and planning for end-stage renal failure. Impaired kidney function has systemic effects on the body. An erythropoietin stimulating agent may be required to ensure adequate production of red blood cells, activated vitamin D supplements and phosphate binders may be required to counteract the effects of kidney failure on bone metabolism, and blood volume and electrolyte disturbance may need correction. Immunosuppression technique can be used in the auto-immune and inflammatory kidney diseases, and other kidney diseases. Currently the related agents are prednisone, mycophenolate, cyclophosphamide, cyclosporine,

tacrolimus, everolimus, thymoglobulin and sirolimus, rituximab, basiliximab and eculizumab, intravenous immunoglobulin, etc.

The end-stage renal failure is a serious disease in the kidney health and the kidney is problem for the physical work in this condition. The end-stage renal failure could be a fatal condition if it cannot do the renal replacement therapy. Dialysis is a strong artificial method to play kidney function by machine when the kidney fails to work. Renal transplantation is to use a health kidney replacing a bad kidney that restores kidney function for the patient. The renal transplantation inserts a healthier kidney into the body from an organ donor which could induce immunologic tolerance of that organ with immunosuppression. Currently, renal transplantation is the most effective treatment for end-stage renal failure although the donor is limited by lack of availability of suitable organs. Common clinical conditions in nephrology are related to the kidney health include the nephritic and nephrotic syndromes, renal cysts, acute kidney injury, chronic kidney disease, urinary tract infection, nephrolithiasis and urinary tract obstruction, etc. Various kidney cancers exist widely. Cancers, cysts, and some other renal conditions can be treated by nephrectomy (removal of the kidney). When renal function, measured by glomerular filtration rate (GFR), is persistently poor, dialysis and kidney transplantation may be considered.

In humans there are two kidneys located in the abdominal cavity (one in left side and the other one in right side of the spine). The asymmetry within the abdominal cavity caused by the position of the liver, typically results in the right kidney being slightly lower and smaller than the left, and being placed slightly more to the middle than the left kidney. Two kidneys work independently. The left kidney is approximately at the vertebral level T12 to L3, and the right one is at the lower location. The right kidney sits just below the diaphragm and posterior to the liver, the left kidney sits below the diaphragm and posterior to the spleen. Resting on top of each kidney is an adrenal gland. The upper parts of the kidneys are partially protected by the eleventh and twelfth ribs. Each kidney together with its adrenal gland is surrounded by two layers of fat (the perirenal and pararenal fat) and the renal fascia. Each adult human kidney weighs about 150 grams in males and about 135 grams in females. Human kidney is about 12 cm length, 6 cm wide and 4 cm thick. The superior border of the right kidney is adjacent to the liver; and the

spleen, for the left kidney. Therefore, both move down on inhalation. If one kidney loses function, the other kidney will increase the renal work, and the working kidney size will increase also.

The parenchyma of the kidney is divided into two major structures: the outer renal cortex and the inner renal medulla, which take the shape of 8 to 18 cone-shaped renal lobes, each containing renal cortex surrounding a portion of medulla called a renal pyramid. Between the renal pyramids are projections of cortex called renal columns. Nephrons, the urine-producing functional structures of the kidney, span the cortex and medulla. The initial filtering portion of a nephron is the renal corpuscle, located in the cortex, which is followed by a renal tubule that passes from the cortex deep into the medullary pyramids. Part of the renal cortex, a medullary ray is a collection of renal tubules that drain into a single collecting duct. The cortex and medulla are the most important tissues in the kidney.

The papilla of each pyramid empties urine into a minor calyx; minor calyces empty into major calyces, and major calyces empty into the renal pelvis, which becomes the ureter. At the hilum, the ureter and renal vein exit the kidney while the renal artery enters. Surrounding these structures is hilar fat and lymphatic tissue with lymph nodes. The hilar fat is contiguous with a fat-filled cavity called the renal sinus. The renal sinus collectively contains the renal pelvis and calyces and separates these structures from the renal medullary tissue. The cortex and medulla play different functions for kidney.

The kidneys receive blood from the left renal artery and right renal artery, which branch directly from the abdominal aorta. Despite their relatively small size, the kidneys receive approximately 20% of the cardiac output in an animal body. Each renal artery branches into segmental arteries, dividing further into interlobar arteries, which penetrate the renal capsule and extend through the renal columns between the renal pyramids. The interlobar arteries then supply blood to the arcuate arteries that run through the boundary of the cortex and the medulla. Each arcuate artery supplies several interlobular arteries that feed into the afferent arterioles that supply the glomeruli.

The medullary interstitium is the functional space in the kidney beneath the individual filters (glomeruli), which are rich in blood vessels. The interstitium absorbs fluid recovered from urine. Various conditions can lead to scarring and congestion of this area, which can cause kidney dysfunction and failure. After

filtration occurs the blood moves through a small network of venules that converge into interlobular veins. As with the arteriole distribution the veins follow the same pattern, the interlobular provide blood to the arcuate veins then back to the interlobar veins, which come to form the renal vein exiting the kidney for transfusion for blood.

The renal artery enters into the kidney at the level of first lumbar vertebra below the superior mesenteric artery. As it enters the kidney it divides into branches, the segmental artery and the interlobar artery. The efferent arterioles leaves the glomerulus and divide into peritubular capillaries that drain into the interlobular veins and then into arcuate vein and then into interlobar vein, which runs into lobar vein, which opens into the segmental vein and they drain into the renal vein, finally from it blood moves into the inferior vena cava. The kidney and nervous system connect through the renal plexus. The plexus's fibers course along the renal arteries to reach each kidney. Input from the sympathetic nervous system triggers vasoconstriction in the kidney, thereby reducing renal blood flow. The kidney also receives input from the parasympathetic nervous system, by way of the renal branches of the vagus nerve. The mammalian kidney develops from intermediate mesoderm. Kidney development (nephrogenesis) proceeds through a series of three successive phases, each marked by the development of a more advanced pair of kidneys.

The kidneys excrete a variety of waste products produced by metabolism into the urine. The ability of mammals and some birds to concentrate wastes into a volume of urine much smaller than the volume of blood from which the wastes are extracted is dependent on an elaborate countercurrent multiplication mechanism. This needs a few independent nephron characteristics to operate, such as a tight hairpin configuration of the tubules, water and ion permeability in the descending limb of the loop, water impermeability in the ascending loop and active ion transport out of most of the ascending limb. In addition, passive countercurrent exchange by the vessels carrying the blood supply to the nephron is essential for enabling this function.

Glucose at normal plasma levels is completely reabsorbed in the proximal tubule. The mechanism for this is the Na⁺/glucose cotransporter. A plasma level of 350 mg/dl will fully saturate the transporters and glucose will be lost in the urine. A plasma glucose level of approximately 160 is sufficient to allow glucosuria, which is an important clinical clue to

diabetes mellitus. Amino acids are reabsorbed by sodium dependent transporters in the proximal tubule. Hartnup disease is a deficiency of the tryptophan amino acid transporter, which results in pellagra. Two organ systems, the kidneys and lungs, maintain acid-base homeostasis, which is the maintenance of pH around a relatively stable value. The lungs contribute to acid-base homeostasis by regulating carbon dioxide (CO₂) concentration. The kidneys have two very important roles in maintaining the acid-base balance: to reabsorb and regenerate bicarbonate from urine, and to excrete hydrogen ions and fixed acids (anions of acids) into urine. Any significant rise in plasma osmolality is detected by the hypothalamus, which communicates directly with the posterior pituitary gland. An increase in osmolality causes the gland to secrete antidiuretic hormone (ADH), resulting in water reabsorption by the kidney and an increase in urine concentration. The two factors work together to return the plasma osmolality to its normal levels.

Although the kidney cannot directly sense blood, long-term regulation of blood pressure predominantly depends upon the kidney. This primarily occurs through maintenance of the extracellular fluid compartment, the size of which depends on the plasma sodium concentration. Renin is the first in a series of important chemical messengers that make up the renin-angiotensin system. Changes in renin ultimately alter the output of this system, principally the hormones angiotensin II and aldosterone. Each hormone acts via multiple mechanisms, but both increase the kidney's absorption of sodium chloride, thereby expanding the extracellular fluid compartment and raising blood pressure. When renin levels are elevated, the concentrations of angiotensin II and aldosterone increase, leading to increased sodium chloride reabsorption, expansion of the extracellular fluid compartment, and an increase in blood pressure. Conversely, when renin levels are low, angiotensin II and aldosterone levels decrease, contracting the extracellular fluid compartment, and decreasing blood pressure. The kidneys secrete a variety of hormones, including erythropoietin, and the enzyme renin. Erythropoietin is released in response to hypoxia (low levels of oxygen at tissue level) in the renal circulation. It stimulates erythropoiesis (production of red blood cells) in the bone marrow. Calcitriol, the activated form of vitamin D, promotes intestinal absorption of calcium and the renal reabsorption of phosphate. Part of the renin-angiotensin-aldosterone system,

renin is an enzyme involved in the regulation of aldosterone levels.

Generally, humans can live normally with just one kidney, as one has more functioning renal tissue than is needed to survive. Only when the amount of functioning kidney tissue is greatly diminished does one develop chronic kidney disease. Renal replacement therapy, in the form of dialysis or kidney transplantation, is indicated when the glomerular filtration rate has fallen very low or if the renal dysfunction leads to severe symptoms. Many renal diseases are diagnosed on the basis of classical clinical findings. A physician (usually a nephrologist) begins by taking a detailed clinical history and performs a physical examination. In addition to medical history and presenting symptoms, a physician will ask about medication history, family history recent infections, toxic/chemical exposures and other historical factors that may indicate an etiology for the patient's renal disease. Often, some diseases are suggested by clinical history and time course alone. For example, in a formerly healthy child with a recent upper respiratory tract infection and facial/lower limb swelling, findings of proteinuria on urinalysis, a diagnosis of minimal change disease is highly suggested. Similarly, a patient with a history of diabetes who presents with decreased urine output is most likely to be suffering from diabetic nephropathy. Often, such cases do not require extensive workup (such as with renal biopsy). A presumptive diagnosis can be made on the basis of history, physical exam and supportive laboratory studies.

Laboratory studies are an important adjunct to clinical evaluation for assessment of renal function. An initial workup of a patient may include a complete blood count (CBC); serum electrolytes including sodium, potassium, chloride, bicarbonate, calcium, and phosphorus; blood urea, nitrogen and creatinine; blood glucose and glycosylated hemoglobin. Glomerular filtration rate (GFR) can be calculated. Urine studies may include urine electrolytes, creatinine, protein, fractional excretion of sodium (FENA) and other studies to assist in evaluation of the etiology of a patient's renal disease. Urinalysis is used to evaluate urine for its pH, protein, glucose, specific gravity and the presence of blood. Microscopic analysis can be helpful in the identification of casts, red blood cells, white blood cells and crystals.

The role of the renal biopsy is to diagnose renal disease in which the etiology is not clear based upon noninvasive means (clinical history,

past medical history, medication history, physical exam, laboratory studies, imaging studies). A detailed description of renal biopsy interpretation is beyond the scope of this article. In general, a renal pathologist will perform a detailed morphological evaluation and integrate the morphologic findings with the clinical history and laboratory data, ultimately arriving at a pathological diagnosis. A renal pathologist is a physician who has undergone general training in anatomic pathology and additional specially training in the interpretation of renal biopsy specimens.

Ideally, multiple core sections are obtained and evaluated for adequacy (presence of glomeruli) intraoperatively. A pathologist/pathology assistant divides the specimen(s) for submission for light microscopy, immunofluorescence microscopy and electron microscopy. The pathologist will examine the specimen using light microscopy with multiple staining techniques (hematoxylin and eosin/H&E, PAS, trichrome, silver stain) on multiple level sections. Multiple immunofluorescence stains are performed to evaluate for antibody, protein and complement deposition. Finally, ultra-structural examination is performed with electron microscopy and may reveal the presence of electron-dense deposits or other characteristic abnormalities that may suggest an etiology for the patient's renal disease.

A pig's kidney opened. In the majority of vertebrates, the mesonephros persists into the adult, albeit usually fused with the more advanced metanephros; only in amniotes is the mesonephros restricted to the embryo. The kidneys of fish and amphibians are typically narrow, elongated organs, occupying a significant portion of the trunk. The collecting ducts from each cluster of nephrons usually drain into an archinephric duct, which is homologous with the vas deferens of amniotes. However, the situation is not always so simple; in cartilaginous fish and some amphibians, there is also a shorter duct, similar to the amniote ureter, which drains the posterior (metanephric) parts of the kidney, and joins with the archinephric duct at the bladder or cloaca. Indeed, in many cartilaginous fish, the anterior portion of the kidney may degenerate or cease to function altogether in the adult.

In the most primitive vertebrates, the hagfish and lampreys, the kidney is unusually simple: it consists of a row of nephrons, each emptying directly into the archinephric duct. Invertebrates may possess excretory organs that are sometimes referred to as "kidneys", but, even

in Amphioxus, these are never homologous with the kidneys of vertebrates, and are more accurately referred to by other names, such as nephridia. The kidneys of reptiles consist of a number of lobules arranged in a broadly linear pattern. Each lobule contains a single branch of the ureter in its center, into which the collecting ducts empty. Reptiles have relatively few nephrons compared with other amniotes of a similar size, possibly because of their lower metabolic rate.

Birds have relatively large, elongated kidneys, each of which is divided into three or more distinct lobes. The lobes consist of several small, irregularly arranged, lobules, each centered on a branch of the ureter. Birds have small glomeruli, but about twice as many nephrons as similarly sized mammals. The human kidney is fairly typical of that of mammals. Distinctive features of the mammalian kidney, in comparison with that of other vertebrates, include the presence of the renal pelvis and renal pyramids, and of a clearly distinguishable cortex and medulla. The latter feature is due to the presence of elongated loops of Henle; these are much shorter in birds, and not truly present in other vertebrates (although the nephron often has a short intermediate segment between the convoluted tubules). It is only in mammals that the kidney takes on its classical "kidney" shape, although there are some exceptions, such as the multilobed reniculate kidneys of pinnipeds and cetaceans. Kidneys of various animals show evidence of evolutionary adaptation and have long been studied in ecophysiology and comparative physiology. Kidney morphology, often indexed as the relative medullary thickness, is associated with habitat aridity among species of mammals. Renal lipid metabolism may play important roles in renal inflammation, glomerulosclerosis and tubulointerstitial injury in diabetic nephropathy (Ma, et al, 2009).

In the United States, nephrology training can be obtained by 1 of the 2 routes. The first is through an internal medicine pathway leading to an internal medicine/nephrology specialty, and sometimes called adult nephrology. The second is through pediatrics leading to a specialty in pediatric nephrology. In the United States, after medical school the adult nephrologists need to complete a three-year residency in internal medicine followed by a two-year (or longer) fellowship in nephrology. A pediatric nephrologist will complete a three-year pediatric residency after medical school or a four-year combined internal medicine and pediatrics

residency, and followed by a three-year fellowship in pediatric nephrology. Once training is successfully completed, the physician is eligible to take the American Board of Internal Medicine (ABIM) or American Osteopathic Board of Internal Medicine (AOBIM) nephrology examination. Nephrologists must pass the examination and be approved by one of the boards. To be approved, the physician must fulfill the requirements for education and training in medicine and nephrology to qualify the taking of the board's examination. If a physician passes the examination, then he (or she) can become a nephrology specialist. Typically, nephrologists also need 2-3 years of training in certain accredited fellowship in nephrology. Only pediatric trained physicians are able to do the pediatric nephrology work, and internal medicine (adult) trained physicians may enter the general adult nephrology fellowships. The International Society of Nephrology is the largest world society in the nephrology major. The National Kidney Foundation is a national organization in the United States. Founded in 1966, the American Society of Nephrology (ASN) is the world's largest professional society in the study of kidney disease.

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