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Question

Explain urine formation and concentration

Formation of urine

There are two kidneys which are bean-shaped and are approximately 10cm long, 5.5cm wide and 3cm thick. Each kidney weighs about 150g and has a marked indentation medially - the hilus - where the renal artery and renal nerves enter and the renal vein and ureter leave. Between them, the kidneys make approximately 30ml or more of urine every hour.

Approximately 25 per cent of the cardiac output goes to the kidneys (McLaren, 1996) where organic waste products are removed in the million or so nephrons (Fig 2) in each kidney. Normal urine production, therefore, depends on normal blood flow to the kidneys. The nephron is the functional unit of the kidney. Nephrons permit the passage of some substances out of the body but restrict the passage of others, for example, blood cells and large proteins.

Filtration

As blood flows through the glomerulus (a capillary network that forms part of the nephron), much of the fluid and waste products in the blood are forced out through the walls of the capillaries, filtered, and then flow into the Bowman's capsule (Fig 2).

The Bowman's capsule is a double-walled endothelial cup that surrounds the glomerulus. This glomerular filtrate (about 125ml per minute) consists of water, glucose, waste salts such as sodium and potassium, and urea. Urea is the most abundant waste product excreted by the kidneys and is formed from ammonia, a highly toxic substance. Ammonia is formed in the liver from the breakdown of amino acids.

Absorption

Much of the glomerular filtrate, including most of the water, is reabsorbed into the capillaries surrounding the proximal and distal convoluted tubules, the loop of Henle and the collecting tubules. All of the glucose will be reabsorbed unless blood glucose levels are high - more than 8.9 millimoles per litre (mmol/l) or 160 milligrams per decilitre (mg/dl) - in which case some glucose will be excreted in the urine.

Sodium is also reabsorbed but the amount varies, depending on how much the body requires to maintain a constant concentration of sodium ions in the blood.

Secretion

This is the final stage of urine formation, and occurs at the distal and collecting tubules. Substances either diffuse or are actively transported out of the capillaries and into the collecting tubules to be excreted in the urine.

Hydrogen ions, potassium ions, ammonia and some drugs are all secreted at this stage and the kidneys play an important role in maintaining the acid-base balance within the body.

Final composition of urine

The final composition of urine is the result of filtration, absorption and secretion by the nephrons. The kidneys produce, on average, one and a half litres of urine each day - this is mostly composed of water, is straw coloured and has a specific gravity of 1.005 to 1.030.

Urea, uric acid, creatinine, sodium chloride and potassium ions are all normal constituents of urine. Blood, ketones and glucose are not, and their presence may indicate disease.

The ureters

Urine passes from the kidneys to the bladder through the ureters where it is stored until it is eliminated via the urethra. Urine is moved along the ureters to the bladder by peristaltic contraction and gravity.

The ureters are muscular tubes about 30cm long. They are firmly attached to the posterior abdominal wall and are retroperitoneal; they do not enter the peritoneal cavity. The ureteral openings into the bladder are flattened (slit-shaped) rather than round. This is due to the oblique angle at which the ureters enter the bladder, which helps to prevent the back-flow of urine into the ureters when the bladder contracts.

Storage of urine

The bladder is a hollow, muscular sac which sits in the pelvis. In males, the base of the bladder lies between the rectum and pubic symphysis while in females the base is below the uterus and anterior to the vagina.

The bladder stores urine and can contain approximately one litre when full. It is held in position by the peritoneum surrounding it (though only its top surface lies within the peritoneum) and by strong umbilical ligaments. The bladder is lined by mucosa. This is particularly thick in the area around the ureter openings and the junction with the urethra, where the mucosa acts as a funnel to channel urine into the urethra when the bladder contracts. During micturition, strong muscles in the bladder walls (the detrusor muscles) compress the bladder, pushing its contents into the urethra.

Control of bladder emptying

The opening, described as the neck of the bladder, between the bladder and the urethra, is closed by two rings of muscle - the internal and external sphincters. The internal sphincter contains smooth muscle fibres and the normal muscle tone of these fibres keeps it contracted; it is therefore not under voluntary control. The external sphincter is formed of a circular band of skeletal muscle which is supplied by the pudendal nerve and is under voluntary control. These fibres remain contracted, as a result of central nervous system stimulation, except during micturition when they relax.

Urine Concentration

The mammalian kidney maintains nearly constant blood plasma osmolality and nearly constant blood plasma sodium concentration by means of mechanisms that independently regulate water and sodium excretion. Because many mammals do not have continuous access to water, the ability to vary water excretion can be essential for survival. Because sodium and its anions are the principal osmotic constituents of blood plasma, and stable electrolyte concentrations are also essential, water excretion must be regulated by mechanisms that decouple it from sodium excretion. The urine concentrating mechanism plays a fundamental role in regulating water and

sodium excretion. When water intake is large enough to dilute blood plasma, a urine more dilute than blood plasma is produced; when water intake is so small that blood plasma is concentrated, a urine more concentrated than blood plasma is produced. In both cases, the total urinary solute excretion rate and the urinary sodium excretion rate are small and normally vary within narrow bounds.

In contrast to solute excretion, urine osmolality varies widely in response to changes in water intake. Following several hours without water intake, such as occurs overnight during sleep, human urine osmolality may rise to ~1,200 mOsm/kg H_2O, about 4-times plasma osmolality (~290 mOsm/kg H_2O). Conversely, urine osmolality may decrease rapidly following the ingestion of large quantities of water, such as commonly occurs at breakfast, human (and other mammals) urine osmolality may decrease to ~50 mOsm/kg H_2O. Most physiologic studies relevant to the urine concentrating mechanism have been conducted in species (rodents, rabbits) that can achieve higher maximum urine osmolalities than humans. For example, rabbits can concentrate to ~1,400 mOsm/kg H_2O, rats to ~3,000 mOsm/kg H_2O, mice and hamsters to ~4,000 mOsm/kg H_2O, and chinchillas to ~7,600 mOsm/kg H_2O.

All mammalian kidneys maintain an osmotic gradient that increases from the cortico-medullary boundary to the tip of the medulla (papillary tip). This osmotic gradient is sustained even in diuresis, although its magnitude is diminished relative to antidiuresis. NaCl is the major constituent of the osmotic gradient in the outer medulla, while NaCl and urea are the major constituents in the inner medulla. The cortex is nearly isotonic to plasma, while the inner medullary (papillary) tip is hypertonic to plasma, and has osmolality similar to urine during antidiuresis. Sodium and potassium, accompanied by univalent anions, and urea are the major urinary solutes; urea is normally predominant urinary solute during a strong antidiuresis.

The mechanisms for the independent control of water and sodium excretion are mostly contained within the renal medulla. The medullary nephron segments and vasa recta are arranged in complex but specific anatomic relationships, both in terms of three-dimensional configuration and in terms of which segments connect to which segments. The production of concentrated urine involves complex interactions among the medullary nephron segmentsmand vasculature. In outer medulla, the thick ascending limbs of the loops of Henle actively reabsorb NaCl. This serves two vital functions: it dilutes the luminal fluid; and it provides NaCl to increase the

osmolality of the medullary interstitium, pars recta, descending limbs, vasculature, and collecting ducts. Both the nephron segments and vessels are arranged in a countercurrent configuration, thereby facilitating the generation of a medullary osmolality gradient along the cortico-medullary axis. In inner medulla, osmolality continues to increase, although the source of the concentrating effect remains controversial. The most widely accepted mechanism remains the passive reabsorption of NaCl, in excess of solute secretion, from the thin ascending limbs of the loops of Henle.

Perfused tubule studies provided the basis for many of the theories of how concentrated urine is produced. The cloning of many of the proteins that mediate urea, sodium, and water transport in nephron segments that are important for urinary concentration and dilution have provided additional insights into the urine concentrating mechanism. In general, the urea, sodium, and water transport proteins are highly specific and appear to eliminate a molecular basis for solvent drag; this specifically suggests that the reflection coefficients should be

General Features of the Concentrating Mechanism

Countercurrent Multiplication

Countercurrent multiplication refers to the process by which a small osmolality difference, at each level of the outer medulla, between fluid flows in ascending and descending limbs of the loops of Henle, is multiplied by the countercurrent flow configuration to establish a large axial osmolality difference. This axial difference is frequently referred to as the cortico-medullary osmolality gradient, as it is distributed along the cortico-medullary axis. A water-impermeable barrier separates the two channels. Vertical arrows indicate flow down the left channel and up the right channel. Horizontal arrows (left-directed) indicate active transport of solute from the right channel to the left channel. Local fluid osmolality is indicated by the numbers within the channels. Successive panels represent the time course of the multiplication process.

Countercurrent Exchange

The blood supply to the medulla, the descending and ascending vasa recta, is arranged in a counter-flow configuration connected by a capillary plexus. Vasa recta achieve osmotic equilibration through a combination of water absorption and solute secretion, as they are freely permeable to water, urea, and sodium. Descending vasa recta loose water and gain solute and while ascending vasa recta gain water and loose solute. The exchange of water and solute between the descending and ascending vasa recta and the surrounding interstitium is called “countercurrent exchange.”