The building up of an osmotic gradient in the kidney medulla is among the most complex mechanisms presented to students of physiology. During lectures, everything seems simple, but reinterpretation is often difficult. Students use different textbooks, but this practice is of limited value, because they often reproduce similar images taken from a common source. This article is an attempt to make the story easier by describing it from another perspective.

DESCRIPTION

The conventional approach is to describe separately the countercurrent multiplier in nephron tubules, the countercurrent exchanger in vasa recta, and the role of collecting ducts (1, 2, 3). Schematic presentations of consecutive steps are often used to explain the development of the osmotic gradient.

In the presented concept, kidney tissue space is considered to be limited, with a positive interstitial hydrostatic pressure. In other words, all of the fluid that goes into the interstitial space must leave it. Any accumulation of fluid would increase the interstitial hydrostatic pressure and compromise kidney architecture and function. Solute and water traffic in described horizons is governed by osmotic forces and by the positive interstitial pressure. Increases in urea availability (diet, etc.), sodium or water depletion, and different circulatory phenomena are all able to modulate this traffic and thus change the resulting osmotic concentration gradients in kidney medulla.

We will try to describe the levels (or horizons) of different osmolarity (as shown in Fig. 1 and cross sections in Fig. 2). Horizon 0 is the cortical level above the medulla with interstitial osmolarity of 300 mOsm/l, containing cortical nephrons with short loops and ordinary peritubular capillaries. In this level, blood flow through the peritubular capillaries washes out any accumulation of interstitial solutes.

Horizons 1–3 contain collecting ducts, tubules, and vasa recta of juxtamedullary nephrons. We can begin with Horizon 1 at the corticomedullary border (interstitial osmolarity of 300–500 mOsm/l). Horizon 2 is deeper in the medulla, with osmolarity of
500 – 800 mOsm/l, whereas Horizon 3 in the inner medulla is the place of urea circulation (800 – 1,200 mOsm/l).

**HORIZON 0**

In the cortical level, blood flows through the net of peritubular capillaries, in which blood is near isosmotic and in equilibrium with the interstitial space, taking out water or solute surplus. Hyperosmolarity coming by interstitial diffusion from the juxtamedullary Horizon 1 is being continuously washed away.

**HORIZON 1**

The interstitial osmotic pressure is 300 – 500 mOsm/l, caused by sodium pumped from the ascending tubule to the interstitial space. The ascending tubule content is of decreasing osmolarity, caused by the pumping process that simultaneously increases osmolarity in the interstitial space. Sodium balance in the Horizon 1 interstitial space is maintained, because sodium entering from the ascending tubule and blood flow in the ascending vasa recta (from deeper medullary horizons) is balanced by sodium removal by blood leaving Horizon 1 via the descending vasa recta and the ascending vasa recta.

Interstitial hyperosmolarity pulls water from descending vasa recta and descending tubule. Both water-permeable structures come from the upper level of less osmolarity. Interstitial water is drawn into the more hyperosmolar content in the ascending vasa recta that comes from the lower and more osmolar levels. Water from the hypotonic content of the collecting duct can enter the interstitium only in the presence of antidiuretic hormone (ADH).

The interstitial hyperosmolarity generated in Horizon 1 spreads to the neighboring levels, up (Horizon 0) and down (Horizon 2).
The situation from Horizon 1 is just accentuated in this more osmotic horizon. Sodium is pumped from the ascending tubule filtrate. Interstitial sodium balances with sodium concentrations in both vasa recta. Water from the descending tubule and from descending vasa recta enters the interstitial space. It is forced to leave by the even more hyperosmotic content in the ascending vasa recta that comes from the lower and more osmolar levels. Water from the hypotonic content of the collecting duct can enter the interstitium only in the presence of antidiuretic hormone ADH. Horizon 2: sodium is pumped out from the ascending tubule. Interstitial sodium balances with sodium concentrations in both vasa recta. Interstitial hyperosmolality pulls water from descending vasa recta and descending tubule. Both water-permeable structures come from the upper level of less osmolarity. Interstitial water is taken out by the more hyperosmolar content in the ascending vasa recta that comes from the lower and more osmolar levels. Water from the hypotonic content of the collecting duct can enter the interstitium only in the presence of antidiuretic hormone ADH. Horizon 3: urea recirculates in the inner medulla, building a stronger osmotic gradient. It enters interstitial space from the collecting duct forced by its concentration gradient, if ADH is present and water is taken out from the collecting duct, building up the urea concentration. Increased interstitial osmolality pulls the remaining water from descending structures. Interstitial water is taken away by the even more osmolar content in the ascending vasa recta.

**HORIZON 2**

The situation from Horizon 1 is just accentuated in this more osmotic horizon. Sodium is pumped from the ascending tubule filtrate. Interstitial sodium balances with sodium concentrations in both vasa recta. Water from the descending tubule and from
descending vasa recta enters the interstitial space. It is
forced to leave by the even more hyperosmotic content in
the ascending vasa recta. ADH is needed to allow water
from collecting ducts to enter the Horizon 2 interstitial
space.

**HORIZON 3**

Urea recirculates in the inner medulla, building a
stronger osmotic gradient. It enters the interstitial
space from the collecting duct, following the con-
centration gradient created by the ADH-sensitive
water reabsorption. Increased interstitial osmolar-
ity pulls the remaining water from the descending
structures. Interstitial water is taken away by the
even more osmolar content in the ascending vasa
recta.

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