The Renal Pelvis: Machinery That Concentrates Urine in the Papilla

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Two decades ago, Bodil Schmidt-Nielsen and Bruce Graves documented the rhythmic contractions of the renal pelvis in a remarkable video, visually demonstrating how peristaltic waves empty the papilla and how the subsequent elastic recoil draws water from the collecting duct and into the tethered-open ascending vasa recta. Thus a periodic hydrostatic gradient generates an axial osmotic gradient. This review recapitulates the video and offers a link to figures and scenes digitized from the original tape.

Surprising to many, the pacemaker for ureteral peristalsis lies within the kidney, near the cortical-medullary junction (3). As a consequence, the renal pelvis (in unipapillate mammals) and the renal calyces (in multipapillate animals) rhythmically contract, forcing blood and fluid from the renal papilla; when the muscle relaxes, fluid and blood return (17). We suggest that the kidney papilla works as a pump, through alternating positive and negative pressures generated by the peristaltic contractions of the pelvic wall. Water moves into the collecting duct cells as a result of the small positive hydrostatic pressure on the walls of the cells, which is generated by the peristaltic wave pushing the fluid through the collecting ducts. Subsequently, fluid moves out of the cells as a result of the negative pressure generated by the elastic forces that expand the papilla during the rebound, and fluid is removed from the interstitium by the vasa recta. This model deals most specifically with mammals that have a relatively long papilla. (The highest degree of urinary concentration is found in mammals with the longest papilla, where peristalsis is expected to have the greatest effect; see Ref. 17).

The structure of the renal pelvis

Mammals and birds are the only vertebrates known to produce a concentrated urine by means of a renal medullary countercurrent system (18). These two countercurrent systems, however, exhibit functional and anatomic differences that appear to be related to the fact that birds excrete uric acid, whereas mammals excrete most of their waste nitrogen in the form of urea. In bird kidneys, there is no urea accumulation in the renal medulla and there is no space for the urine to contact the renal medulla, because the medulla is surrounded by tight sheets of connective tissue. In mammalian kidneys, urea accumulation in the renal medulla plays an important role in the mechanism that concentrates the urine in the collecting ducts. Furthermore, the mammalian renal medulla is surrounded by a muscular funnel-shaped pelvic wall (Fig. 1A), which leaves an elaborate urinary space between the renal medulla and the inside of the pelvic wall. At this point, clarification concerning terminology is necessary. In the kidney with many papillae, such as human kidneys, each papilla is surrounded by a funnel-shaped calyx. This compartment is not present in kidneys with one papilla. In the human kidney, it is the compartment between the calyces and the ureter that is called the pelvis. This compartment is not present in kidneys with one papilla, where the pelvis is a direct extension of the ureter.

A plexus of smooth muscle fibers is found in the wall of both renal pelvis and calyces. Two distinct layers exist in unipapillate kidneys. The inner layer contains fibers that run in assorted directions, insert near the site where the pelvic wall joins with the base of the papilla, and are continuous with the ureteral smooth muscle; the outer layer is richly innervated but is more diffuse and covers only the renal pelvis, connecting places with the inner layer but finally ending abruptly at the juncture with the ureter (Fig. 2A; Ref. 7). Although the layers of smooth muscle in the caliceal wall in multipapillate kidneys are not as distinct (Fig. 2B), the inner fibers tend to insert near the juncture of the caliceal wall and the base of the papilla, whereas the outer fibers extend further (the muscular levator fornices; Ref. 15), forming a thickened ring around the tubules and vasa recta that course toward the papilla (the Ringmuskel der Papille; Ref. 10). The smooth muscles continue as far as the connective tissue associated with the arterial arteries and veins (peripapillary fibers; Ref. 16). A coordinated peristaltic contraction of these smooth muscles can thus exert a rhythmic pumping action on the entire renal medulla, a function first proposed by Henle (10) as a mechanism to promote the emptying of those tubules located in the renal papilla.
The mammalian renal pelvis makes it possible for urine to contact the epithelium covering the inner and outer renal medulla. In cross-sections of unipapillate mammalian kidneys, the pelvis appears to surround the inner medulla only and to have a simple funnel shape. Casts of the pelvic urinary space, however, reveal the presence of a series of leaf-like extensions (Fig. 1B). There is an enormous variation in pelvic spaces, which range from the simple funnel shape to the most elaborate of pelvic extensions. Secondary pouches and fornices are found in all types of mammalian kidney. They are urinary spaces in which the urine can contact the very thin epithelium covering outer medullary tissue (see Ref. 13). In a simple cross-section schematic of the rodent kidney, the inner medulla and papilla can be seen to be hanging within the pelvic space. Adjacent to the renal medulla is the septum, which is continuous with the ureter. Each septum has a series of spokes that radiate toward the cortex and form the fornices. Between the spokes, the outer margin of the septum is free and has a semilunar edge. Behind this edge the secondary pouches extend between these capillaries and the urine reaching the pelvic extensions. The elaborate fornices in the sand rat maximize the possibility for exchange of water and solutes between the urine in the pelvis and the capillaries in the outer medulla. However, there is no evidence to suggest that the ability to concentrate the urine is enhanced in the mammals with the most elaborate and complex pelvic extensions. Rather, these structures allow the animals to respond to water intoxication by rapidly flattening the solute gradient along the renal papilla (17).

Urodynamic events occur in the renal pelvis

"The renal pelvis is not a rigid and motionless hollow space. This fact has been known for over 55 years...." (15), and that was written in 1940! The hamster is particularly well suited for observation of urodynamic events in the renal pelvis because it has a single, rather long papilla. After careful removal of several layers of fat and connective tissue, the muscular constrictions of the peripelvic wall become visible, particularly when the papilla is transilluminated by a fiberoptic light. In the hamster, the rate of peristaltic contractions is normally 13/min (17), compared with 7/min in miniature swine (but 12–13/min in isolated swine kidney; Refs. 4 and 20), 0.3/min in dog (but 13–17/min in isolated canine kidney; Refs. 3 and 6), and 0.3/min in humans (2). This peristalsis has a profound effect on the size and shape of the papilla. As the wall contracts, the papilla narrows. Its diameter is reduced by as much as 20%, which means that the cross-sectional area is reduced by as much as 36%. At the moment the peristaltic wave moves past its tip, the papilla rebounds upward. The average movement is ~300 μm (17).

Smooth muscle is found in the wall of the renal pelvis up to the base of the papilla in both unipapillate and multipapillate kidneys but is not found in the papilla itself (Fig. 2). The peristaltic contractions are controlled by a pacemaker situated in the uppermost parts of the pelvis (9), which overrides the slower rhythms intrinsic to sections of the pelvic wall and ureter.

It is possible to study the movement of the urine in the collecting ducts and in the pelvic space surrounding the renal papilla during the peristaltic contractions of the muscular pelvic wall by using a technique introduced by Steinhausen in 1964 (19). When the dye Lissamine Green SF is injected intravenously, it quickly reaches the capillaries of the kidney and is filtered by the glomeruli. It soon appears in the proximal tubules on the cortical surface of the kidney. As it moves through the proximal tube convolutions, the color fades from the first convolutions as the dye enters the loops of Henle. The colored fluid then returns to the distal tubules. Since there has been water reabsorption from the renal...
tubules, the dye is more concentrated and appears darker. A similar sequence is seen in the kidney papilla. The dye first appears in the capillaries and the vasa recta. After it has been filtered and moved through the proximal convolutions, it appears in the loops of Henle. Gradually the dye is cleared from the loops, and after it has moved through the distal tubules it enters the collecting tubules and the collecting ducts. If dye is infused continuously, the urine moving through the collecting ducts will remain green.

Urine can reflux into the renal pelvis?

Urine leaving the ducts of Bellini at the tip of the papilla will generally flow directly down the ureter after each pelvic contraction. Occasionally, however, urine fans out around the tip of the papilla, briefly bathing the lower 50 mm with urine (17). This pattern, which we call tip reflux, is seen during constant or decreasing urine flow. When the urine flow rate is rapidly increasing, however, a different flow pattern is seen. The urine no longer flows directly down the ureter as it leaves the ducts of Bellini. Instead the urine is swept up into the pelvis, where it reaches all the fornices and secondary pouches. During the next contraction, the urine is swept down over the papilla and enters the ureter. This pattern we call full pelvic reflux.

Full pelvic refluxes are physiologically induced when the rate of urine flow increases faster than 0.05 μl/min². They continue for several minutes after the flow rate is no longer increasing. During rising urine flow, the urine becomes more dilute and its osmolality decreases. The urine being swept up into the pelvic extensions thus has a lower osmolality than the papillary tissue. It has been shown that full pelvic reflexes, under these circumstances, serve to reduce the osmolality and urea concentration of the renal medulla. As a consequence, the pelvic reflexes may serve to shorten the time it takes for a water diuresis to develop following a large intake of water. This may be particularly useful for desert animals that drink large amounts of water periodically and therefore have to be able to dilute the urine promptly to avoid water intoxication (17).

Peristalsis transports urine as a bolus down the ureter

Anyone who has passed a kidney stone knows that the ureter also contracts peristaltically. Urine entering the ureter is propelled toward the bladder in boluses, the ureter being closed in front of, and behind, each bolus. At low urine flow rates, the boluses are short; at higher flow rates, the boluses become longer but the linear velocity of the boluses is unchanged. Thus the flow in the ureter is very different from flow in a pipe with a fixed diameter, where the linear velocity would change in direct proportion to the flow rate. As the urine flow increases further, the lengths of the boluses continue to increase until the ureter is filled from one end to the other (17).

Peristaltic forces concentrate urine

As the peristaltic wave moves down over the renal papilla,
the urine is pushed through the papillary collecting ducts as a bolus. Light micrographs of the papilla fixed during contraction show that the collecting ducts are closed (Fig. 3A) but that they are wide open when the pelvic wall is relaxed (Fig. 3B). As with the ureter, the collecting ducts are normally empty and closed behind the bolus. The bolus is short during low urine flow rates; the collecting ducts remain empty until the next bolus is pushed through. At low urine flow rates, they may be empty as much as 95% of the time, with fluid being in contact with the collecting duct epithelium only briefly. The linear velocity of the peristaltic wave is 1.6 mm/s and equals the velocity of the short bolus. At higher urine flow rates, the bolus is longer because the velocity of the leading edge, which is determined by the urine production, is lower than the velocity of the peristaltic wave pushing the trailing edge; at the highest flow rates, the collecting ducts remain empty until the peristaltic wave moves over the papilla. Thus, paradoxically, the contact time is prolonged (or the average linear velocity of the urine in the collecting ducts is slower) at higher flow rates compared with low urine flow rates.

As the peristaltic contraction moves down the papilla, the collecting duct fluid is pushed through the ducts at a velocity greater than the velocity with which the fluid is formed, thus increasing the hydrostatic pressure on the wall of the ducts. During low rates of urine production, only half of the fluid in the terminal collecting duct exits the papilla from the ducts of the urine. The remaining volume is absorbed into the collecting duct epithelial cells, whose volumes are increased by approximately the volume of the fluid absorbed from the collecting duct lumen during each peristaltic contraction. As the contraction passes, collecting ducts close behind the urine bolus (17).

Ostia of the ducts of Bellini are normally patent (Fig. 3C) but frequently appear to contain prolapsed medullary tissue in kidneys from obese rabbits (Fig. 3D), obesity being characterized by a modest degree of arterial hypertension (+11 mmHg in these rabbits and similar elevations in obese dogs and humans), an elevated renal interstitial hydrostatic pressure (26 vs. 9 mmHg in obese vs. lean dogs), and a markedly expanded inner medullary interstitium (in rabbit, dog, and humans; Ref. 5). Thus the expanded interstitium may provide a greater than normal resistance to the peristaltic rush of fluid through the collecting ducts, which increases the interstitial pressure in the renal parenchyma and results in an increased arterial pressure systemically as well as prolapse of medullary contents out the ostia.

The loops of Henle are also partly emptied during the pelvic contraction. This can be seen following a bolus injection of Lissamine Green SF, when the fluid in the loops becomes temporarily green. Each contraction appears to squeeze the fluid out of the loops, with some fluid being pushed retrograde and the remainder toward the tip.

FIGURE 3. Structural changes during and after a peristaltic contraction. A: renal papilla during a peristaltic contraction. The renal papilla of a Syrian hamster was snared at a location ~1 mm from its tip during the contraction phase of the pelvic peristalsis. The collecting ducts are closed (17). B: renal papilla between peristaltic contractions. Similarly, a papilla was snared during the relaxation phase, showing the collecting ducts to be open, the cells to be smaller in volume, and spaces to be present between the cells of the collecting ducts (17). C: patent ducts of Bellini. Ducts of Bellini are generally patent, as shown by these in a rabbit papilla (tissue was pressure perfused and examined with a scanning electron microscope; Ref. 5). D: prolapsed ducts of Bellini. In obese rabbits, the ducts of Bellini are often seen distended by tissue prolapsed from within the papilla (5). A and B are reprinted from Kidney International, volume 22, pages 613-625, 1982. C and D are reprinted from Ref. 5, with permission.
The peristaltic contractions of the pelvic wall profoundly affect the papillary blood flow. The papilla inside the pelvic wall becomes pale as the wall contracts around it, with the capillaries narrowing during each contraction. With close observation under the microscope, it can be seen that the blood flow periodically stops and then briefly moves retrograde in descending capillaries. Measurements have shown that blood flow is stopped ~30% of the time. Light and electron micrographs from renal papillae fixed at the very end of contraction have shown that capillaries, as well as the loops of Henle and the collecting ducts, were all tightly closed, whereas those from relaxed papillae were all open. This intermittent pattern of flow may help preserve the osmotic gradient along the renal papilla, since a continuous flow would result in increased removal of papillary solutes (17).

Papilla rebound moves water into the vasa recta

The peristaltic contraction both compresses and stretches the papilla, causing it to become longer and narrower. During the early relaxation period (1 s), the papilla rebounds to its shorter and broader relaxed form. The collecting ducts initially remain closed, but water moves out of the cells into the interstitium due to negative hydrostatic pressure generated by the elastic properties of the interstitial matrix. Since the ascending vasa recta are tethered to other structures, they are opened as the tissue expands during rebound, permitting water to enter (14). Soon blood returns to the vasa recta, first to the descending and then to the ascending vasa recta, pushing along the column of water that had entered the vasa recta from the interstitium. At this time, tubular fluid also returns to the loops of Henle.

In late relaxation (2 s), collecting ducts open as urine flows into them from above. The remaining structures continue to function normally, with the shape of the papilla unchanged, the vasa recta open with blood flow, and the loops of Henle open with fluid continuing to flow through them.

The pelvic wall is necessary for peristalsis

If the pelvic wall is resected, the blood flow in the capillaries is continuous and the flow in the loops of Henle and through the collecting ducts is also uninterrupted. Similarly, if an intact pelvis is paralyzed by local anesthetic, the ureteral peristalsis becomes uncoupled from the pelvis and the pelvis becomes paralyzed. The flows in the collecting ducts, loops of Henle, and vasa recta are now continuous, as it is when the pelvic wall is removed or paralyzed. Physiological findings have shown that, when the pelvic wall is removed or paralyzed, the osmolality and sodium concentration of the papillary tissue decreases significantly (17).

Mechanisms that concentrate urine in the papilla

To concentrate the urine in the collecting ducts, water must be removed from the collecting ducts in excess of solutes. Part of this water removal is caused by the accumulation of solutes in the papillary interstitium, a consequence of ion transport that occurs in the outer medulla. Mathematical models, however, cannot explain the actual concentrations reached in some animals (12, 13). The model presented here (Fig. 4) proposes that the hydrostatic pressure generated by the pelvic wall peristalsis contributes to the removal of water from the collecting duct lumen in four steps. First, the force of the peristaltic contraction moves the bolus of urine not only down the collecting duct but also into the cells lining the duct (Fig. 4A). Second, negative interstitial pressures that develop during rebound tend to move water from the epithelial cells into the interstitium. Third, the tethered ascending vasa recta tend to open before other structures (Fig. 4B; Ref. 14), generating a negative intravascular hydrostatic force and drawing interstitial fluid into the lumen. Fourth, the ascending vasa recta has an unusually large hydraulic permeability and low reflection coefficient to albumin (14), allowing for vascular uptake of both large and small osmotically active particles. Together, these four steps constitute a highly effective mechanism for the
movement of interstitial fluid out of the medulla for any given hydrostatic or osmotic gradient.

The structure of the model is unlike other mechanisms that have been proposed. Most importantly, it is not a continuous function of time; instead, the physical consequences of the renal pelvic contractions must be integrated over a complete peristaltic cycle for the transport of water to occur. Second, the thermodynamic energy is not derived from ATP or ionic gradients within the papilla. This is fortunate, because the tissue would appear to have meager energy reserves: blood flow is slow, the partial pressure of oxygen is low (<10 Torr), mitochondria are few, and most energy is derived from anaerobic glycolysis (8). Instead, we propose that the thermodynamic energy is derived from an external source, namely the contraction of smooth muscle in the richly vascularized wall of the renal pelvis. Third, certain proposed mechanisms require that the interstitial compartments have a fixed volume or that the renal papilla have a low compliance (12, 14). In fact, the renal papilla must be very compliant, having no capsule and little collagen. Instead, we propose that periodic contractions of the renal pelvic wall enforce a constant volume, rhythmically moving fluid from the collecting ducts into the ascending vasa recta.

This model does not deal explicitly with the loops of Henle, although their contents are emptied by peristalsis much as the collecting ducts. Neither does it deal with the transport of solutes, nor the dynamic effect of the repeated movements of pure water into the papillary interstitium at the mouths of the aquaporin channels, a flux that may alter the physical-chemical nature of the proteins, hyaluronan, and proteoglycans that fill that space. We anticipate that application of contemporary techniques will begin to elucidate these features of renal urodynamical activity.

A supplemental video, “Renal Pelvis” by Bruce Graves and Bodil Schmidt-Nielsen, is available online for browsing. It can be accessed through the APS website (http://www.apsarchive.org/renalpelvis/index.htm). The text has been transcribed, and figures or short clips can be downloaded by double-clicking the icons. A DVD version is also available from The American Physiological Society; contact subscrip@the-aps.org or (301) 634-7180 to order.

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References