Fig. 8.1. Glomerular filtration barrier. The glomerular filtration barrier consists of the capillary endothelial cell, the glomerular basement membrane, and the epithelial cells (podocytes). H₂O and most solutes pass through fenestrations in the endothelial cells, through a semipermeable basement membrane, through the slit pores between the foot processes of the podocytes, into Bowman’s space, and then into the proximal renal tubule.

Fig. 8.2. Major physiologic processes of renal tubules that pertain to solutes and H₂O. The solute concentrations are provided to illustrate changes that occur as the fluid moves through the nephron (see Fig. 8.3). Actual solute concentrations would vary, depending on many physiologic and pathologic factors.

Fig. 8.2. continued

- The osmolality of the plasma and the ultrafiltrate are equal (near 300 mmol/kg) as H₂O and nonprotein solutes pass through the glomerular filtration barrier.
- In the proximal tubules, a majority of the H₂O and solutes that enter the tubules are resorbed through active, facilitated, and passive processes. The osmolality of the tubular fluid leaving the proximal tubule is still near 300 mmol/kg, but the fluid volume is greatly diminished.
- In the ascending limb of the loop of Henle, tubular fluid is concentrated and volume reduced by the passive movement of H₂O. Urea may diffuse from the interstitial fluid to the tubular fluid. At the bottom of the loop of Henle, the concentration of the tubular fluid will vary among species. The 1500 mmol/kg value is probably appropriate for horses and cattle, whereas the solute concentration in cats may be 2400 mmol/kg.
- In the ascending limb of the loop of Henle, solutes (mostly Na⁺, Cl⁻, and K⁺) passively leave the tubular fluid via a Na⁺-K⁺-2Cl⁻ carrier (energy provided by Na⁺-K⁺-ATPase pump in the basolateral membrane), but H₂O remains. Thus, the tubular fluid becomes dilute, and the fluid leaving the diluting segment has an osmolality near 100 mmol/kg. Passive fCa²⁺ and fMg²⁺ resorption depends on an electrical gradient promoted by the Na⁺-K⁺-2Cl⁻ cotransporter and the recycling of K⁺, whereas active fCa²⁺ and fMg²⁺ resorption is promoted by PTH.
- In the distal and collecting tubules, there are multiple processes involved in electrolyte balance, acid-base balance, and conservation of H₂O (see the text for specifics). The major actions of ADH are to promote resorption of H₂O and urea. The major actions of aldosterone are the resorption of Na⁺ and Cl⁻ and the secretion of K⁺ and H⁺. The osmolality of the urine typically is > 600 mmol/kg and may be > 2000 mmol/kg.
- In most healthy domestic mammals, the net function of a nephron is to excrete urea, Crt, K⁺, H⁺, NH₃⁺, and PO₄ and to conserve Na⁺, Cl⁻, HCO₃⁻, fCa²⁺, fMg²⁺, glucose, amino acids, and H₂O. The equine nephron excretes fCa²⁺ instead of conserving it.
- The table in the top of the figure shows a comparison of the approximate solute concentrations (in terms of osmolality and USG) in different segments of a functional nephron. Note that the USG for plasma (1.028–1.034) were determined by using a refractometer’s urine specific gravity scale. The true specific gravity of the plasma would be nearer 1.018–1.022, and such a range has little to no clinical relevance. ⊗, ATPase pump; ∥, transporter or shuttle.

Fig. 8.3. Osmolality changes in a healthy mammal’s nephron. (Details of the movement of solute and H₂O in nephrons are described in Fig. 8.2.) The ultrafiltrate formed by glomerular filtration of plasma has an osmolality near 300 mmol/kg. As fluid moves through the proximal convoluted tubule (PCT), the H₂O and solutes are resorbed. Because resorption is isosmotic, the tubular fluid’s osmolality does not change. However, there are marked changes in osmolality during fluid transit through the loop of Henle (LoH). When fluid leaves the LoH, the tubular fluid’s osmolality is near 100 mmol/kg. Minimal change in osmolality occurs in the distal tubule (DT) as electrolytes are resorbed. In the absence of ADH activity, H₂O remains in the collecting tubules, and thus the nephron produces hyposthenuric urine (typically USG < 1.007). With minimal ADH activity in healthy mammals, the nephron produces isosthenuric urine (typically USG of 1.007–1.013). With marked ADH activity in the collecting tubules, a large portion of the H₂O is resorbed to form maximal concentration. The maximal concentrating ability varies among domestic mammals. The right y-axis is probably appropriate for horses and cattle (i.e., maximum USGmax = 1.050), whereas other y-axes are needed for dogs (> 1.800 mmol/kg or USGmax = 1.800) and cats (> 2400 mmol/kg or USGmax = 1.880)

Fig. 8.4. Graphical representation of the effects of chronic renal disease and progressive dysfunction on an animal’s urine volume and serum concentrations of UN or Crt. Shaded grey areas represent the reference intervals for urine volume (top bar) and for the [UN] or [Crt] (bottom bar). The patient’s urine volume and [UN] or [Crt] are represented by labeled dashed lines. A theoretical maximal urine volume line is shown to illustrate that animals with polyuric renal failure do not produce maximal urine volume.

- In stage 1 (diminished renal reserve), progressive renal disease is destroying nephrons and thus GFR decreases. However, there is still sufficient function to clear urea and Crt adequately, and thus the animal is not azotemic. Also, there is sufficient ability to concentrate urine, and thus polyuria is absent or not detected. As the renal dysfunction approaches stage 2, a mild polyuria may develop because of impaired concentrating ability.
- In stage 2 (renal insufficiency), there is sufficient loss of nephrons so that the renal concentrating ability is decreased (isosthenuria and polyuria develop) and the excretion of urea and Crt by the kidneys is insufficient. As the renal dysfunction approaches stage 3 (end-stage renal disease, oliguric or anuric renal failure), only a few nephrons are filtering plasma, and thus a marked azotemia develops.
- In stage 4 (end-stage renal disease, oliguric or anuric renal failure), only a few nephrons are filtering plasma, and thus a marked azotemia develops. The animal also becomes oliguric or anuric because very little plasma H₂O enters the kidney. The remaining tubules cannot concentrate or dilute the filtrate, and thus USGmax will reflect isosthenuria.

Fig. 8.5. Physiologic processes or concepts concerning urea and Crt. Urea synthesis occurs in hepatocytes via the urea cycle, which is one method of incorporating NH₃⁺ into molecules for excretion of excess NH₄⁺ that is formed in tissues or intestine. After urea passively enters plasma from hepatocytes, it has two possible fates.

- Urea passes freely across the glomerular filtration barrier and is excreted in urine or resorbed by renal tubules: 50–65 % of urea present in glomerular filtrate is resorbed in proximal and collecting tubules. Urea resorption in proximal tubules is enhanced by H₂O resorption in proximal tubules and by increased ADH activity in the medullary collecting ducts.
- Urea enters the intestinal tract of monogastric mammals (via the blood or the biliary system), where it is degraded by enteric bacteria (with urease), passively absorbed into portal blood, or excreted in feces. In cattle, urea enters the rumen (via saliva and blood), where it is degraded to NH₃⁺. Crt is the product of creatine (not Crt) degradation. Creatine phosphate serves as a high-energy molecule for muscle contractions (creatine + ATP ↔ creatine + ADP). Crt enters the plasma after the degradation of creatine or creatine PO₄ in muscle fibers (the animal’s muscle or dietary meat). Crt is excreted from the body via the kidneys and intestine.
- Crt is also excreted or degraded in feces of people and in saliva of cattle. Alimentary tract excretion is suspected to occur in dogs, cats, and horses, as Crt is diffusible across most cell membranes.

Fig. 8.6. Illustration of scales in a Leica TS400 hand-held refractometer. The refractometer measures the fluid’s refractive index, and the urine specific gravity and serum plasma protein scales are used to estimate USGmax or total protein concentrations, respectively. The refractometer scales were calibrated for human samples. Image used with permission from Leica Microsystems, Buffalo, NY. PR/N ratio 6.54, conversion factor—6.54 g of protein contains 1 g of nitrogen.
Fig. 8.7. Illustration of scales in a Leica VET 360 hand-held veterinary refractometer. The refractometer has a specific gravity scale for dog and large animal urine and a separate scale for cat urine. Note that, for a given refractive index, the specific gravity for cat urine is greater than the specific gravity for dog or large animal urine. Image used with permission from Leica Microsystems, Buffalo, NY.

Fig. 8.8. Comparison of osmolality and USG \( r_{\text{USG}} \) in canine urine samples with USG \( r_{\text{USG}} \leq 1.025 \) (\( n = 185 \)). There is a high correlation \( (r = 0.91) \) between the two methods of assessing urine solute concentration: freezing-point osmometry and refractive index. For these samples, the mean Osm : USG \( r_{\text{USG}} \) was 33 with a sd of 5; the mean ± 2 sd (or 95 % interval) is represented by the area between the two diagonal lines. The three values that fell above the 95 % interval had high protein concentrations (estimated concentration ≥ 500 mg/dL).

Fig. 8.9. Four major types of proteinuria.
- In prerenal proteinurias (Prerenal), small proteins (e.g., hemoglobin dimers, light chains, and myoglobin) present in the plasma at increased concentrations are excreted in the urine because they pass through the glomerular filtration barrier and are incompletely resorbed in tubules.
- In glomerular proteinurias (Glom.), glomerular disease damages the filtration barrier and decreases selective permeability. Glomeruli become increasingly permeable to larger or negatively charged plasma proteins. These proteins pass through the defective filtration barrier and are incompletely resorbed by tubules, so they are excreted in urine.
- In tubular proteinurias (Tubular), proximal renal tubules are defective, so proteins that normally are resorbed from ultrafiltrate (e.g., some albumin and smaller globulins) are not, and thus they are excreted in the urine.
- In hemorrhagic and inflammatory proteinurias (Hemor. & Inf.), plasma proteins or hemoglobin enter the urine because of hemorrhage or inflammation involving the renal tubules, renal pelvis, ureters, urinary bladder, urethra, or genital tract tissues.

Fig. 8.10. Protein-losing nephropathy and renal failure. Illustrations depict a body’s extracellular fluid as a lake, kidneys as a dam, and the urine as the river below the dam. Urea and Crt molecules are small fish in the lake, and albumin molecules are big fish. The nephron consists of the sieve or filter at the lake outlet and the tubes that run through the dam. Some H\(_2\)O and urea are reclaimed to maintain extracellular fluid H\(_2\)O and urea content. Only one of ten nephrons is shown as a filter with a connected tubular system.
- In healthy animals, urea and Crt pass freely through ten functional filters, into the dam’s tubes, and into the river. Some urea (and H\(_2\)O) is reclaimed from the dam’s tubes in a process enhanced by ADH. Albumin is too big to pass through the filters, so it stays in the lake.
- In the protein-losing nephropathy illustration, 40 % of the filters (and nephrons) have been destroyed. The remaining 60 % are damaged, more porous, and allow albumin to enter the dam and river. The loss of albumin from the lake causes hypoalbuminemia and proteinuria. The remaining filters are sufficient to keep urea and Crt removed from the lake, and thus azotemia does not develop.
- In protein-losing nephropathy and renal failure, 80 % of the filters (and nephrons) have been destroyed. The remaining 20 % are damaged, more porous, and allow albumin to enter the dam and river. The loss of albumin from the lake causes hypoalbuminemia and proteinuria. The remaining filters are insufficient to keep urea and Crt removed from the lake, and thus azotemia develops. Also, the remaining nephrons cannot adequately conserve H\(_2\)O, and thus polyuria develops.