error of 9 L. One consequence of a filtration-reabsorption design is that regulation has to have exquisite fidelity, and even small errors are not tolerated.

Filtration

Filtration occurs exclusively at the glomerulus. The GFR, measured as volume per unit time, has been the standard quantitative surrogate for overall kidney function, although there are many disturbances of renal function that are not associated with a decrease in GFR (e.g., nephrotic syndrome, tubulointerstitial disorders, kidney stones). Numerically, GFR can be conceptualized as an equation:

$$GFR = K_f \times (\Delta P - \Delta \Pi)$$

where the ultrafiltration coefficient, K_f, is equal to the surface area for filtration multiplied by the hydraulic permeability; the hydrostatic driving force, ΔP, is the pressure gradient between the glomerular capillary and Bowman's space, which drives fluid to go into Bowman's space to form urine; and the osmotic driving force, $\Delta \Pi$, is the osmotic pressure gradient between the glomerular capillary and Bowman's space, which holds fluid back in the capillary and slows down filtration.

Many renal diseases affect the determinants of GFR. Glomerular disease (see Chapter 28) decreases K_f by affecting both the surface area for filtration and the hydraulic permeability. Changes in ΔP are commonly involved in diseases that reduce GFR. Changes in renal blood flow and more importantly in afferent and efferent arteriolar resistances can drastically affect ΔP and GFR. Functional changes in ΔP, such as prerenal failure from hypoperfusion or hepatorenal syndrome (see Chapter 31), can radically lower GFR simply by hemodynamic changes without any structural glomerular lesions. Changes in $\Delta \Pi$ also can affect GFR but have not been studied in as much detail.

Reabsorption

High GFR, which is required to maintain a high metabolic rate, can be sustained only if there is high reclamation to maintain intravascular volume and prevent circulatory collapse. Tubular reabsorption thwarts the loss of valuable solutes and allows for finer tuning of the water and solutes not reabsorbed. The resulting tubular contents are excreted. In the mammalian kidney, tubular reabsorption assumes critical roles in the regulation of excretion of many solutes (Table 25-2). A universal mechanism of reabsorption is energy-dependent transepithelial transport, which is mostly Na^+ dependent but can be Na^+ independent. The proximal tubules participate in the reabsorption of all solutes, but some solutes are sequentially reabsorbed by the proximal and distal segments; in these cases, the generic design tends to be high-capacity reabsorption proximally and more of a high-gradient reabsorption for fine tuning distally. The axial difference

TABLE 25-2 SOLUTE EXCRETION

SOLUTE	FILTRATION	REABSORPTION	SECRETION	FE (%)	REGULATION
Water	Yes	Yes	No	0.3-6.0	Responds primarily to body tonicity but also EABV. ADH is the major regulator of collecting duct water permeability.
Na^+	Yes	Yes	No	0.2-2.0	Responds to EABV. Reabsorption is stimulated by sympathetic nerves, angiotensin II, aldosterone; inhibited by atrial natriuretic peptides, dopamine, uroguanylin.
K^+	Yes	Yes	Yes	5-20	Responds to total body potassium status. Secretion is controlled primarily by aldosterone and distal Na^+ delivery.
Ca^{2+}	Yes	Yes	No	2-10	Responds to serum ionized $[Ca^{2+}]$ and body need for calcium. Major calciotropic hormones include parathyroid hormone, vitamin D, and calcitonin. Renal epithelia directly respond to ionized calcium via the calcium sensing receptor.
Mg^{2+}	Yes	Yes	No	3-5	Responds to total body magnesium status and requirements. Paracrine regulation is via epidermal growth factor.
HCO_3^-	Yes	Yes	Yes	0.1-0.5	Most bicarbonate reabsorption is to reclaim the filtered load. Responds to systemic acid-base status which can be mediated by direct sensing by the renal epithelia or via hormonal actions (e.g., angiotensin II, endothelin). Bicarbonate can also be secreted in the collecting duct when alkali excretion is required.
Phosphate	Yes	Yes	No	5-20	Responds to serum phosphate concentration and body phosphate status. Reabsorption primarily resides in the proximal tubule and is regulated by parathyroid hormone and fibroblast growth factor-23.
Glucose	Yes	Yes	No	0.2-0.5	The proximal tubule reclaims almost all filtered glucose except when the filtered load exceeds reabsorptive capacity. The cortical proximal tubule performs gluconeogenesis from other organic substrates.
Uric acid	Yes	Yes	Yes	10-50	Major routes of uric acid clearance are (1) renal excretion and (2) intestinal secretion and uricolysis. Handling of both secretion and reabsorption in the proximal tubule is complex, and regulatory mechanisms are unclear.
Creatinine	Yes	No	Yes	1.0-1.2	Filtered at the glomerulus and secreted by the proximal tubule. The contribution of the tubules to creatinine clearance increases when GFR declines.

ADH, Antidiuretic hormone; EABV, effective arterial blood volume; FE, fractional excretion under normal physiology.