1. The answer is D [V B 4 b]. Distal K⁺ secretion is decreased by factors that decrease the driving force for passive diffusion of K⁺ across the luminal membrane. Because spironolactone is an aldosterone antagonist, it reduces K⁺ secretion. Alkalosis, a diet high in K⁺, and hyperaldosteronism all increase [K⁺] in the distal cells and thereby increase K⁺ secretion. Thiazide diuretics increase flow through the distal tubule and dilute the luminal [K⁺] so that the driving force for K⁺ secretion is increased.

2. The answer is D [I C 2 a; VII C; Figure 5-15; Table 5-6]. After drinking distilled water, subject A will have an increase in intracellular fluid (ICF) and extracellular fluid (ECF) volumes, a decrease in plasma osmolarity, a suppression of antidiuretic hormone (ADH) secretion, and a positive free-water clearance (\( C_{\text{H₂O}} \)), and will produce dilute urine with a high flow rate. Subject B, after drinking the same volume of isotonic NaCl, will have an increase in ECF volume only and no change in plasma osmolarity. Because subject B's ADH will not be suppressed, he will have a higher urine osmolarity, a lower urine flow rate, and a lower \( C_{\text{H₂O}} \) than subject A.

3. The answer is A [IX D 1 a–c; Tables 5-8 and 5-9]. An acid pH, together with decreased HCO₃⁻ and decreased PCO₂, is consistent with metabolic acidosis with respiratory compensation (hyperventilation). Diarrhea causes gastrointestinal (GI) loss of HCO₃⁻, creating a metabolic acidosis.

4. The answer is D [IX D 1 a–c; Tables 5-8 and 5-9]. The decreased arterial [HCO₃⁻] is caused by gastrointestinal (GI) loss of HCO₃⁻ from diarrhea, not by buffering of excess H⁺ by HCO₃⁻. The woman is hyperventilating as respiratory compensation for metabolic acidosis. Her hypokalemia cannot be the result of the exchange of intracellular H⁺ for extracellular K⁺, because she has an increase in extracellular H⁺, which would drive the exchange in the other direction. Her circulating levels of aldosterone would be increased as a result of extracellular fluid (ECF) volume contraction, which leads to increased K⁺ secretion by the distal tubule and hypokalemia.

5. The answer is C [II C 4, 5]. Glomerular filtration will stop when the net ultrafiltration pressure across the glomerular capillary is zero; that is, when the force that favors filtration (47 mm Hg) exactly equals the forces that oppose filtration (10 mm Hg + 37 mm Hg).

6. The answer is D [IX C 1 a–b]. Decreases in arterial PCO₂ cause a decrease in the reabsorption of filtered HCO₃⁻ by diminishing the supply of H⁺ in the cell for secretion into the lumen. Reabsorption of filtered HCO₃⁻ is nearly 100% of the filtered load and requires carbonic anhydrase in the brush border to convert filtered HCO₃⁻ to CO₂ to proceed normally. This process causes little acidification of the urine and is not linked to net excretion of H⁺ as titratable acid or NH₄⁺.

7. The answer is B [II C 1]. To answer this question, calculate the glomerular filtration rate (GFR) and \( C_x \). \( \text{GFR} = 150 \text{ mg/mL} \times 1 \text{ mL/min} ÷ 1 \text{ mg/mL} = 150 \text{ mL/min} \). \( C_x = 100 \text{ mg/mL} \times 1 \text{ mL/min} ÷ 2 \text{ mg/mL} = 50 \text{ mL/min} \). Because the clearance of X is less than the clearance of inulin (or GFR), net reabsorption of X must have occurred. Clearance data alone cannot determine whether there has also been secretion of X. Because GFR cannot be measured with a substance that is reabsorbed, X would not be suitable.

8. The answer is A [IX C 2]. Total daily production of fixed H⁺ from catabolism of proteins and phospholipids (plus any additional fixed H⁺ that is ingested) must be matched by the sum of excretion of H⁺ as titratable acid plus NH₄⁺ to maintain acid–base balance.
9. The answer is C [I B 1 a]. Mannitol is a marker substance for the extracellular fluid (ECF) volume. ECF volume = amount of mannitol/concentration of mannitol = 1 g - 0.2 g/0.08 g/L = 10 L.

10. The answer is D [III B; Figure 5-5]. At concentrations greater than at the transport maximum \( T_m \) for glucose, the carriers are saturated so that the reabsorption rate no longer matches the filtration rate. The difference is excreted in the urine. As the plasma glucose concentration increases, the excretion of glucose increases. When it is greater than the \( T_m \), the renal vein glucose concentration will be less than the renal artery concentration because some glucose is being excreted in urine and therefore is not returned to the blood. The clearance of glucose is zero at concentrations lower than at \( T_m \) (or lower than threshold) when all of the filtered glucose is reabsorbed, but is greater than zero at concentrations greater than \( T_m \).

11. The answer is D [VII D; Table 5-6]. A person who produces hyperosmotic urine (1000 mOsm/L) will have a negative free-water clearance \(-C_{H_2O} = V - C_{osm}\). All of the others will have a positive \( C_{H_2O} \) because they are producing hyposmotic urine as a result of the suppression of antidiuretic hormone (ADH) by water drinking, central diabetes insipidus, or nephrogenic diabetes insipidus.

12. The answer is A [IX B 3]. The Henderson–Hasselbalch equation can be used to calculate the ratio of \( HA/A^- \):

\[
\begin{align*}
\text{pH} &= \text{pK} + \log \frac{A^-}{HA} \\
7.4 &= 5.4 + \log \frac{A^-}{HA} \\
2.0 &= \log \frac{A^-}{HA} \\
100 &= \frac{A^-}{HA} \text{ or } \frac{HA}{A^-} = 1/100
\end{align*}
\]

13. The answer is A [II C 3; IV C 1 d (2)]. Increasing filtration fraction means that a larger portion of the renal plasma flow (RPF) is filtered across the glomerular capillaries. This increased flow causes an increase in the protein concentration and oncotic pressure of the blood leaving the glomerular capillaries. This blood becomes the peritubular capillary blood supply. The increased oncotic pressure in the peritubular capillary blood is a driving force favoring reabsorption in the proximal tubule. Extracellular fluid (ECF) volume expansion, decreased peritubular capillary protein concentration, and increased peritubular capillary hydrostatic pressure all inhibit proximal reabsorption. Oxygen deprivation would also inhibit reabsorption by stopping the \( Na^+-K^+ \) pump in the basolateral membranes.

14. The answer is E [I B 2 b–d]. Interstitial fluid volume is measured indirectly by determining the difference between extracellular fluid (ECF) volume and plasma volume. Inulin, a large fructose polymer that is restricted to the extracellular space, is a marker for ECF volume. Radioactive albumin is a marker for plasma volume.

15. The answer is D [III C; Figure 5-6]. At plasma concentrations that are lower than at the transport maximum \( T_m \) for para-aminohippuric acid (PAH) secretion, PAH concentration in the renal vein is nearly zero because the sum of filtration plus secretion removes virtually all PAH from the renal plasma. Thus, the PAH concentration in the renal vein is less than that in the renal artery because most of the PAH entering the kidney is excreted in urine. PAH clearance is greater than inulin clearance because PAH is filtered and secreted; inulin is only filtered.

16. The answer is E [VII D; Figures 5-14 and 5-15]. The person with water deprivation will have a higher plasma osmolarity and higher circulating levels of antidiuretic hormone (ADH). These effects will increase the rate of \( H_2O \) reabsorption in the collecting ducts and create a negative free-water clearance \(-C_{H_2O}\). Tubular fluid/plasma (TF/P) osmolarity in the proximal tubule is not affected by ADH.

17. The answer is C [II C 4; Table 5-3]. Dilution of the afferent arteriole will increase both renal plasma flow (RPF) [because renal vascular resistance is decreased] and glomerular
filtration rate (GFR) [because glomerular capillary hydrostatic pressure is increased]. Dilatation of the efferent arteriole will increase RPF, but decrease GFR. Constriction of the efferent arteriole will decrease RPF (due to increased renal vascular resistance) and increase GFR. Both hyperproteinemia (↑π in the glomerular capillaries) and a ureteral stone (↑ hydrostatic pressure in Bowman's space) will oppose filtration and decrease GFR.

18. The answer is B [IX D 4; Table 5-8]. First, the acid–base disorder must be diagnosed. Alkaline pH, low PCO₂, and low HCO₃⁻ are consistent with respiratory alkalosis. In respiratory alkalosis, the [H⁺] is decreased and less H⁺ is bound to negatively charged sites on plasma proteins. As a result, more Ca²⁺ is bound to proteins and, therefore, the ionized [Ca²⁺] decreases. There is no respiratory compensation for primary respiratory disorders. The patient is hyperventilating, which is the cause of the respiratory alkalosis. Appropriate renal compensation would be decreased reabsorption of HCO₃⁻, which would cause his arterial [HCO₃⁻] to decrease and his blood pH to decrease (become more normal).

19. The answer is C [VII B, D 4; Table 5-6]. Both individuals will have hyperosmotic urine, a negative free-water clearance (–CH₂O), a normal corticopapillary gradient, and high circulating levels of antidiuretic hormone (ADH). The person with water deprivation will have a high plasma osmolarity, and the person with syndrome of inappropriate antidiuretic hormone (SIADH) will have a low plasma osmolarity (because of dilution by the inappropriate water reabsorption).

20. The answer is B [Table 5-11]. Thiazide diuretics have a unique effect on the distal tubule; they increase Ca²⁺ reabsorption, thereby decreasing Ca²⁺ excretion and clearance. Because parathyroid hormone (PTH) increases Ca²⁺ reabsorption, the lack of PTH will cause an increase in Ca²⁺ clearance. Furosemide inhibits Na⁺ reabsorption in the thick ascending limb, and extracellular fluid (ECF) volume expansion inhibits Na⁺ reabsorption in the proximal tubule. At these sites, Ca²⁺ reabsorption is linked to Na⁺ reabsorption, and Ca²⁺ clearance would be increased. Because Mg²⁺ competes with Ca²⁺ for reabsorption in the thick ascending limb, hypermagnesemia will cause increased Ca²⁺ clearance.

21. The answer is D [IX D 2; Table 5-8]. First, the acid–base disorder must be diagnosed. Alkaline pH, with increased HCO₃⁻ and increased PCO₂, is consistent with metabolic alkalosis with respiratory compensation. The low blood pressure and decreased turgor suggest extracellular fluid (ECF) volume expansion and increased intracellular H⁺ to leave cells in exchange for extracellular K⁺. The appropriate respiratory compensation is hypoventilation, which is responsible for the elevated PCO₂. H⁺ excretion in urine will be decreased, so less titratable acid will be excreted. K⁺ secretion by the distal tubules will be increased because aldosterone levels will be increased secondary to ECF volume contraction.

22. The answer is B [VII B; Figure 5-14]. This patient’s plasma and urine osmolarity, taken together, are consistent with water deprivation. The plasma osmolarity is on the high side of normal, stimulating the posterior pituitary to secrete antidiuretic hormone (ADH). Secretion of ADH, in turn, acts on the collecting ducts to increase water reabsorption and produce hyperosmotic urine. Syndrome of inappropriate antidiuretic hormone (SIADH) would also produce hyperosmotic urine, but the plasma osmolarity would be lower than normal because of the excessive water retention. Central and nephrogenic diabetes insipidus and excessive water intake would all result in hyposmotic urine.

23. The answer is C [II B 2, 3]. Effective renal plasma flow (RPF) is calculated from the clearance of para-aminohippuric acid (PAH) \[C_{PAH} = \frac{U_{PAH}}{P_{PAH} \times V} = 600 \text{ mL/min}\]. Renal blood flow (RBF) = RPF/1 – hematocrit = 1091 mL/min.

24. The answer is A [III D]. Para-aminohippuric acid (PAH) has the greatest clearance of all of the substances because it is both filtered and secreted. Inulin is only filtered. The other substances are filtered and subsequently reabsorbed; therefore, they will have clearances that are lower than the inulin clearance.
25. The answer is D [I C 2 f; Table 5-2]. By sweating and then replacing all volume by drinking H$_2$O, the woman has a net loss of NaCl without a net loss of H$_2$O. Therefore, her extracellular and plasma osmolality will be decreased, and as a result, water will flow from extracellular fluid (ECF) to intracellular fluid (ICF). The intracellular osmolality will also be decreased after the shift of water. Total body water (TBW) will be unchanged because the woman replaced all volume lost in sweat by drinking water. Hematocrit will be increased because of the shift of water from ECF to ICF and the shift of water into the red blood cells (RBCs), which causes their volume to increase.

26. The answer is A [Table 5-4]. Exercise causes a shift of K$^+$ from cells into blood. The result is hyperkalemia. Hyposmolality, insulin, β-agonists, and alkalosis cause a shift of K$^+$ from blood into cells. The result is hypokalemia.

27. The answer is E [Table 5-9]. A cause of metabolic alkalosis is hyperaldosteronism; increased aldosterone levels cause increased H$^+$ secretion by the distal tubule and increased reabsorption of "new" HCO$_3^-$; Diarrhea causes loss of HCO$_3^-$ from the gastrointestinal (GI) tract and acetazolamide causes loss of HCO$_3^-$ in the urine, both resulting in hyperchloremic metabolic acidosis with normal anion gap. Ingestion of ethylene glycol and salicylate poisoning leads to metabolic acidosis with increased anion gap.

28. The answer is A [VI B; Table 5-7]. Parathyroid hormone (PTH) acts on the renal tubule by stimulating adenyl cyclase and generating cyclic adenosine monophosphate (cAMP). The major actions of the hormone are inhibition of phosphate reabsorption in the proximal tubule, stimulation of Ca$^{2+}$ reabsorption in the distal tubule, and stimulation of 1,25-dihydroxycholecalciferol production. PTH does not alter the renal handling of K$^+$.

29. The answer is C [IV C 3 b; V B 4 b]. Hypertension, hypokalemia, metabolic alkalosis, elevated serum aldosterone, and decreased plasma renin activity are all consistent with a primary hyperaldosteronism (e.g., Conn's syndrome). High levels of aldosterone cause increased Na$^+$ reabsorption (leading to increased blood pressure), increased K$^+$ secretion (leading to hypokalemia), and increased H$^+$ secretion (leading to metabolic alkalosis). In Conn's syndrome, the increased blood pressure causes an increase in renal perfusion pressure, which inhibits renin secretion. Neither Cushing's syndrome nor Cushing's disease is a possible cause of this patient's hypertension because serum cortisol and adrenocorticotropic hormone (ACTH) levels are normal. Renal artery stenosis causes hypertension that is characterized by increased plasma renin activity. Pheochromocytoma is ruled out by the normal urinary excretion of vanillylmandelic acid (VMA).

30. The answer is D [IX D 3; Tables 5-8 and 5-9]. The history strongly suggests chronic obstructive pulmonary disease (COPD) as a cause of respiratory acidosis. Because of the COPD, the ventilation rate is decreased and CO$_2$ is retained. The [H$^+$] and [HCO$_3^-$] are increased by mass action. The [HCO$_3^-$] is further increased by renal compensation for respiratory acidosis (increased HCO$_3^-$ reabsorption by the kidney is facilitated by the high PCO$_2$).

31. The answer is B [IX D 4; Table 5-8]. The blood values in respiratory alkalosis show decreased PCO$_2$ (the cause) and decreased [H$^+$] and [HCO$_3^-$] by mass action. The [HCO$_3^-$] is further decreased by renal compensation for chronic respiratory alkalosis (decreased HCO$_3^-$ reabsorption).

32. The answer is E [IX D 1; Tables 5-8 and 5-9]. In patients who have chronic renal failure and ingest normal amounts of protein, fixed acids will be produced from the catabolism of protein. Because the failing kidney does not produce enough NH$_4^+$ to excrete all of the fixed acid, metabolic acidosis (with respiratory compensation) results.

33. The answer is E [IX D 1; Tables 5-8 and 5-9]. Untreated diabetes mellitus results in the production of ketoacids, which are fixed acids that cause metabolic acidosis. Urinary excretion of NH$_4^+$ is increased in this patient because an adaptive increase in renal NH$_3$ synthesis has occurred in response to the metabolic acidosis.
34. **The answer is A** [IX D 2; Tables 5-8 and 5-9]. The history of vomiting (in the absence of any other information) indicates loss of gastric H+ and, as a result, metabolic alkalosis (with respiratory compensation).

35. **The answer is E** [V B 4]. K+ is secreted by the late distal tubule and collecting ducts. Because this secretion is affected by dietary K+, a person who is on a high-K+ diet can secrete more K+ into the urine than was originally filtered. At all of the other nephron sites, the amount of K+ in the tubular fluid is either equal to the amount filtered (site A) or less than the amount filtered (because K+ is reabsorbed in the proximal tubule and the loop of Henle).

36. **The answer is D** [VII B 3; Figure 5-16]. A person who is deprived of water will have high circulating levels of antidiuretic hormone (ADH). The tubular fluid/plasma (TF/P) osmolality is 1.0 throughout the proximal tubule, regardless of ADH status. In antidiuresis, TF/P osmolarity > 1.0 at site C because of equilibration of the tubular fluid with the large corticopapillary osmotic gradient. At site E, TF/P osmolarity > 1.0 because of water reabsorption out of the collecting ducts and equilibration with the corticopapillary gradient. At site D, the tubular fluid is diluted because NaCl is reabsorbed in the thick ascending limb without water, making TF/P osmolarity < 1.0.

37. **The answer is E** [IV A 2]. Because inulin, once filtered, is neither reabsorbed nor secreted, its concentration in tubular fluid reflects the amount of water remaining in the tubule. In antidiuresis, water is reabsorbed throughout the nephron (except in the thick ascending limb and cortical diluting segment). Thus, inulin concentration in the tubular fluid progressively rises along the nephron as water is reabsorbed, and will be highest in the final urine.

38. **The answer is A** [IV A 2]. The tubular fluid inulin concentration depends on the amount of water present. As water reabsorption occurs along the nephron, the inulin concentration progressively increases. Thus, the tubular fluid inulin concentration is lowest in Bowman’s space, prior to any water reabsorption.

39. **The answer is A** [IV C 1 a]. Glucose is extensively reabsorbed in the early proximal tubule by the Na+-glucose cotransporter. The glucose concentration in tubular fluid is highest in Bowman’s space before any reabsorption has occurred.

40. **The answer is C** [IV A 2]. Once inulin is filtered, it is neither reabsorbed nor secreted. Thus, 100% of the filtered load of inulin remains in tubular fluid at each nephron site and in the final urine.

41. **The answer is A** [IV C 1 a]. Alanine, like glucose, is avidly reabsorbed in the early proximal tubule by a Na+-amino acid cotransporter. Thus, the percentage of the filtered load of alanine remaining in the tubular fluid declines rapidly along the proximal tubule as alanine is reabsorbed into the blood.

42. **The answer is D** [III C; IV A 3]. Para-aminohippuric acid (PAH) is an organic acid that is filtered and subsequently secreted by the proximal tubule. The secretion process adds PAH to the tubular fluid; therefore, the amount that is present at the end of the proximal tubule is greater than the amount that was present in Bowman’s space.

43. **The answer is B** [III E]. Alkalization of the urine converts more salicylic acid to its A− form. The A− form is charged and cannot back-diffuse from urine to blood. Therefore, it is trapped in the urine and excreted.