Solutions to Test Your Knowledge: Hyponatremia

1. D. All of the above
Most patients with euvoletic hyponatremia will have the syndrome of inappropriate secretion of anti-diurectic hormone (SIADH). This diagnosis requires documentation of euvoletic with less than maximal urinary dilution in the absence of decreased kidney function, glucocorticoid deficiency, and hypothyroidism.

2. C. Less than 12 mEq/L over the first 24 hrs, and <18 mEq/L over the first 48 hrs
Sterns and colleagues examined the safe rate of correction in patients with [Na+] <105 mEq/L. This group showed that neurologic sequelae of hyponatremia treatment only occurred when hyponatremia was corrected too rapidly. They demonstrated that no patients developed neurologic sequelae (which includes osmotic demyelination) when chronic hyponatremia was corrected <12 mEq/L over the first 24 hrs and <18 mEq/L over the first 48 hrs. These are limits and not goals of correction. It is believed that a more modest rate of 6 mEq/L/day provides a better safety margin in most cases. Furthermore, this group reported that no patient with acute hyponatremia developed neurologic sequelae.

3. A. Increased plasma tonicity AND B. Decreased intravascular volume
The main physiologic stimuli for the release of AVP are an increase in plasma tonicity and a decrease in intravascular volume. Studies have implicated the organum vasculosum of the lamina terminalis (OVLT), which lacks a blood–brain barrier, as well as areas of the adjacent hypothalamus near the anterior wall of the third cerebral ventricle, as the site of the principal brain osmoreceptors. Osmoreceptor cells in the brain primarily respond to plasma tonicity rather than to total plasma osmolality. The physiologic relevance of this finding is that osmoreceptors function primarily to preserve cell volume; elevations of solutes that cross cellular membranes such as urea, unlike elevations of sodium, do not cause cellular dehydration and therefore do not activate the mechanisms that defend body fluid homeostasis by preserving or increasing body water stores. The cellular osmosensing mechanism utilized by the OVLT cells is an intrinsic depolarizing receptor potential. This potential is generated through a molecular transduction complex by the transient receptor potential vaniloid (TRPV) family of cation channel proteins. These channels are generally activated by cell membrane stretch to cause a nonselective conductance of cations, with a preference for Ca^{2+}. 
4. C. SIADH
SIADH is the main indication for the use of the vaptan class of drugs. Vaptans are contraindicated in hypovolemic hyponatremia. The treatment for this condition is volume repletion. Concomitant use of vaptans and hypertonic saline increases the risk of neurologic sequelae related to osmotic demyelination. In post-marketing surveillance, two reports of osmotic demyelination have been reported, with both instances occurring when a vaptan was administered concomitantly or in close proximity to hypertonic saline. Vaptans should not be relied upon for the correction of hyponatremia when severe neurologic symptoms are present. In this instance, hypertonic saline is preferred. However, this has not been studied in any randomized fashion.

5. A. True
The vaptan class of drugs is generally considered to be safe and well tolerated. However, thirst (9%), increased urinary frequency (9.9%), and dry mouth were more commonly observed in the vaptan treated groups. In the TEMPO trial for the use of tolvaptan in ADPKD, it was noted tolvaptan treated patients had increases in uric acid (6.2% vs. 1.7%), and significant ALT or AST elevations (4.7% vs. 1.7%).