Solutions to Test Your Knowledge: Central Diabetes Insipidus

1. D: Langerhans cell histiocytosis
2. D: Carbidopa
3. D: Lung (small cell) cancer
4. B: An increase in serum sodium from 138 to 149 mmol/L after overnight water restriction, with an AM urine specific gravity of <1.005 that rises to 1.030 after administration of desmopressin.

1D. Langerhans cell histiocytosis. Congenital syndromes effecting the development of the pituitary gland tend to cause the absence of ADH secretion leading to congenital central diabetes insipidus. Wolfram syndrome, an autosomal recessive disorder, is otherwise called *DIDMOAD* syndrome, which includes diabetes insipidus, diabetes mellitus, optic atrophy, and deafness. Septo-optic dysplasia is a complex cerebral developmental disorder involving the fore brain and pituitary, leading to decreased ADH production and sometimes disrupted thirst mechanism causing dangerously elevated sodium levels. Similarly, posterior pituitary ectopia results from impaired development of the posterior pituitary and can cause decreased ADH production. Langerhans cell histiocytosis, on the other hand, leads to infiltrative degeneration of the stalk of the pituitary causing a central diabetes insipidus. It is not a congenital cause, but rather a complication of a systemic disease.

2D. Carbidopa. While desmopressin is the most commonly used treatment for central diabetes insipidus, other therapies have been proposed. Some of these are also used in treatment of nephrogenic diabetes insipidus.

Chlorthalidone is a thiazide diuretic which helps in concentrating the urine in the distal convoluted tubule by inhibiting the re-absorption of Na and Cl. It increases the urine osmolality in patients with central diabetes insipidus who have absent or very low levels of circulating ADH. *Chlorpropamide* is an oral hypoglycemic agent which is now rarely used for the treatment of diabetes mellitus. However, one of side effects is hyponatremia, which is useful as treatment in central diabetes insipidus. Although the mechanism is unclear, there have been a couple of theories postulated: one being that it increases the medullary hypertonicity and the other being that it increases the water permeability of the collecting duct. *Carbamazepine*, which is used in the treatment of seizure and mood disorders, has also shown some efficacy in the treatment of central diabetes insipidus by exerting inherent antidiuretic properties along with increasing the response of ADH in the kidneys. *Indomethacin* inhibits the production of prostaglandins, which are known to be inhibitory to ADH activity. The usage of indomethacin in conjunction with thiazide diuretics have shown to reduce urine output by 25-50%. These drugs are assumed to be effective when there is a partial central diabetes insipidus with still some amount of circulating ADH. *Carbidopa* is used in the treatment of Parkinson disease and has no role in the treatment of central diabetes insipidus.

3D. Lung (small cell) cancer. Anorexia nervosa is associated with abnormal ADH secretory patterns and can cause diabetes insipidus. Sarcoidosis causes infiltration of the pituitary by granulomas, leading to central diabetes insipidus. Craniopharyngioma, a neoplasm of the pituitary gland embryonic tissue, causes central diabetes insipidus and adipsic hypernatremia. Hypoxic ischemic

encephalopathy from prolonged cardio-pulmonary resuscitation causes injury to the posterior pituitary leading to decreased ADH release and excessive polyuria. On the contrary, small cell carcinoma of the lung is notorious in causing SIADH as a paraneoplastic syndrome, leading to hyponatremia.

4B. An increase in serum sodium from 138 to 149 mmol/L after overnight water restriction with an AM urine specific gravity of <1.005 that rises to 1.030 after administration of desmopressin.

The first case depicts a case of primary polydipsia or psychogenic polydipsia. In this case, the patient's urine osmolality increases appropriately with water restriction, reflecting an intact ADH secretory mechanism. Further administration of desmopressin does not increase urine osmolality. It is also to be noted that patients with psychogenic polydypsia may wash out some of the medullary concentrating gradient due to chronic water overload, and hence cannot concentrate their urine to more than 500-600 mOsmol/Kg.

In the second scenario, the patient's sodium has risen after an overnight water restriction, but his urine specific gravity remains dilute. This signifies a defect in appropriate secretion (or) action of ADH. Administration of desmopressin increased urine specific gravity/osmolality helps us determine that the defect is central, with defective ADH secretion. The last scenario shows a minimal response to administration of desmopressin, suggesting a diagnosis of nephrogenic diabetes insipidus.