Posterior Pituitary  
(Neurohypophysis)  
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Learning Objectives

1. Understand factors controlling the release of vasopressin.
2. Know major causes of vasopressin deficiency (diabetes insipidus).
3. Understand pathophysiology of polyuria and its clinical investigation.
4. Know major causes and pathophysiology of the syndrome of inappropriate secretion of antidiuretic hormone (SIADH).
5. Understand how to diagnose the syndrome of inappropriate secretion of ADH.
6. Know major actions of oxytocin and factors responsible for its release.

POSTERIOR PITUITARY  
(NEUROHYPOPHYSIS)

Vasopressin and oxytocin are the only hormones known to be secreted by the neurohypophysis in humans. Human vasopressin is called arginine vasopressin (AVP) to distinguish it from lysine vasopressin in pigs. It is also called antidiuretic hormone (ADH), which reflects its major physiologic action. These hormones are nonapeptides (nine amino acids) with similar primary structures but very different biological and immunological properties. They are characterized by a ring structure with disulfide (S-S) linkage (Figure 1).

\[
\text{Cys - Tyr - Ile - Gln - Asn - Cys - Pro - Leu - Gly - NH}_2
\]

Oxytocin

\[
\text{Cys - Tyr - Phe - Gln - Asn - Cys - Pro - Arg - Gly - NH}_2
\]

Arginine vasopressin

Figure 1: Structures of oxytocin and vasopressin

The posterior lobe of the pituitary gland is an extension of the forebrain. Figure II shows the neuroanatomical relationship of the posterior pituitary in man.
The major site of AVP and oxytocin synthesis is in the magnocellular neurons of the supraoptic and paraventricular nuclei of the hypothalamus. These hormones are biosynthesized in different cell bodies by way of macromolecular precursors that are cleaved to yield the active hormone, a linking protein called neurophysin, and other peptides. These products are stored in vesicles at the end of neurosecretory axons in the neurohypophysis and secreted by a calcium-dependent process of exocytosis.

**Figure 2:** Schematic presentation of hypothalamus, posterior pituitary, and surrounding structures. Four major neuronal tracts arise from the supraoptic and paraventricular nuclei, which pass to the posterior lobe of the pituitary, the median eminence, the brain stem and spinal cord, and the forebrain. Afferent fibers to these nuclei originate from the osmoreceptors and baroreceptors, the latter passing via brain stem nuclei.

**VASOPRESSIN**

**Actions:** AVP plays important role in volume regulation, sodium homeostasis, regulation of serum osmolality, and possibly also learning and memory modulation. Three receptor subtypes that mediate the actions of AVP have been identified (V(1A), V(2) and V(1B)). The cardiovascular and renal effects of AVP are mediated primarily by V(1A) and V(2) receptors, respectively. High concentrations of AVP acting on V(1A) receptors cause vasoconstriction, as may occur in response to severe hypotension or to infusion of vasopressin for treatment of bleeding esophageal varices. Antagonism of V(1A) receptors results in vasodilatation. Activation of V(1A) receptors located in the myocardium results in increased afterload and hypertrophy. The V(1B) receptors, located in the anterior pituitary and median eminence, mediate ACTH release. Furthermore, AVP, perhaps from axons that terminate in the cerebrum, may play a role in learning and memory. Via actions of its V2 receptors in the distal renal collecting tubules, AVP conserves water and concentrates the urine by enhancing the hydro-osmotic flow of water from the luminal fluid through the cells of the collecting tubule of the kidney to the medullary
interstitium. This action assists in maintaining constancy of the osmolality and volume of body fluids. Antagonism of V(2) receptors in the distal renal tubules results in aquarexia or free water excretion.

Normal hormone levels and metabolism: The AVP concentration of blood fluctuates, with a maximum late at night and in the early morning and a minimum in the early afternoon. Under conditions of random fluid intake peripheral plasma AVP concentration in humans ranges from 2.5 to 8 ng/l. Inactivation of AVP occurs largely in liver and kidneys. Approximately 7 to 10 percent of secreted AVP is excreted in the urine as active hormone.

Control of AVP release: The release of AVP is influenced by a number of stimuli (Figure 3).

1) Osmoregulation: Under normal conditions AVP release is primarily regulated by osmoreceptors in the hypothalamus. Increases in plasma osmolality cause shrinkage of the osmoreceptor cells, which in turn alter the electric activity of the neurons and increase AVP release. As plasma AVP rises, antidiuresis and urinary concentrations increase. The servomechanism between effective plasma osmolality and AVP release normally maintains plasma osmolality within a very narrow range of 280 to 296 mOsm/kg.

2) Volume regulation: Decreases in plasma volume, through effects on stretch receptors in the left atrium and perhaps in the pulmonary veins, stimulate the release of AVP by reducing the tonic inhibitory pulses from the left atrium to the hypothalamus. The neural impulses travel via the vagi to the reticular formation of midbrain and diencephalon and hence to the supraoptic and paraventricular nuclei, where they are integrated with the other stimuli that affect AVP release.

3) Baroreceptor regulation: Activation of carotid and aortic baroreceptors in response to hypotension causes release of AVP. Hypotension due to blood loss is the most potent stimulus and may raise plasma levels of AVP to 1000 times normal. These concentrations of AVP may cause marked vasoconstriction, which probably plays a role in the restoration of blood pressure.

4) Neural regulation: Both cholinergic and beta-adrenergic stimuli release AVP, while atropine and alpha-adrenergic stimulation inhibit AVP release, apparently by actions on the hypothalamus. Emotional stress, nausea, vomiting and pain may stimulate AVP secretion.

5) Aging: The aging process (i.e., over 60 years old) is associated with enhanced AVP release in response to a rising plasma osmolality and a progressive increase in plasma AVP concentration. These physiological changes appear to place the older individual under greater risk of developing water retention and hyponatremia.

6) Pharmacologic influences: A large number of pharmacologic agents can stimulate or inhibit AVP release. Nicotine stimulates and ethanol inhibits AVP release.

7) AVP response to water deprivation and to water load: Water deprivation provides both an osmotic and a volume stimulus to vasopressin release by increasing plasma osmolality and decreasing plasma volume. In contrast, the administration of water lowers plasma osmolality and expands blood volume, inhibiting the release of AVP.
Interaction of osmotic and volume influences: Osmotic factors ordinarily control the release of AVP; however, larger changes in blood volume (i.e., more than 10%) may blunt and eventually overcome the osmotic influences. Hypotension can activate arterial baroreceptors and exert a powerful stimulus to the elaboration of AVP and thus override simultaneous inhibiting influences.

Relation between AVP release and thirst: Under normal conditions there is close coordination between AVP release and thirst, both of which are ordinarily regulated by small changes in plasma osmolality. There is a progressive increase in thirst with increasing plasma osmolality, and onset of thirst occurs at values similar to the threshold for vasopressin release. Decreased arterial blood volume also stimulates both thirst and AVP release. Angiotensin II is a potent dipsogen (i.e., stimulates thirst) which can also stimulate vasopressin secretion and it is increased in response to volume depletion.

Figure 3: Schematic representation of the control of AVP release and cellular action of AVP. OC=optic chiasm. MB=mammillary body.

Effects of glucocorticoids: Cortisol and the posterior pituitary have antagonist effects on water excretion. Cortisol elevates the osmotic threshold for AVP release and can also act directly on the renal tubules to increase solute-free water excretion in the urine. The subnormal ability to dilute the urine in patients with adrenal insufficiency is due to the decreased level of cortisol, as well as excessive secretion of vasopressin due to volume contraction and decrease osmotic threshold.
(11) Cellular mechanism of AVP activity: The action of AVP on renal tubular cells is through V2 receptors and activation of adenylate cyclase to increase intracellular cAMP and enhance water permeability. Its action on vascular smooth muscle is through V1 receptors by stimulating influx of calcium ions into cells and vasoconstriction.

(12) Aquaporins: The aquaporins are channels that mediate water traffic from the lumen of the renal tubules into the plasma compartment. The aquaporin family contains more than a dozen members, many of which are expressed in the kidneys but also at other sites including the central nervous system. In the kidney, at least 7 aquaporins are expressed at distinct sites. AQP1 in the proximal tubule and descending limb mediates urine concentration. AQP2 is localized to the principal cells of the connecting tubule and collecting duct and is the major mediator of vasopressin action in the kidney. [Indeed, AQP2 is the predominant vasopressin-regulated water channel.] AQP3 and AQP4 expressed in the basolateral plasma membrane of collecting duct cells transport the water molecules that have been reabsorbed via AQP2 into plasma. Additional aquaporins in the kidney (AQP6, AQP7, AQP8) are expressed at varying levels in proximal tubules and collecting duct cells, but their function has not been elucidated. Body water balance is tightly regulated by vasopressin, and multiple studies now have underscored the essential roles of AQP2 in this. Vasopressin acutely regulates the permeability of the distal collecting duct principally by upregulating the translocation of AQP2 from intracellular vesicles to the apical plasma membrane. Lack of functional AQP2 leads to congenital or primary forms of diabetes insipidus; reduced expression or impaired translocation of AQP2 may be the underlying mechanism for acquired nephrogenic diabetes insipidus, postobstructive polyuria, and several disorders associated with impaired urine concentration (including renal failure). The reverse is also true: conditions associated with water retention (congestive heart failure, pregnancy, and SIADH) often are accompanied by increased expression of AQP2 and increased translocation to the apical plasma membrane.

DEFICIENCY OF VASOPRESSIN OR CENTRAL DIABETES INSIPIDUS

Central diabetes insipidus, known also as neurogenic DI, is a disorder defined by failure to concentrate urine as a result of decreased secretion of osmoregulated AVP. Polyuria, throughout the day and night, is a prominent clinical failure, and, as patients rely on their intact thirst mechanism to maintain water balance, thirst or polydipsia is a major complaint. A preference for ice-cold water is expressed by some patients. The disorder is uncommon, and its incidence has been estimated at 1 in 25,000.

Etiology: Neurogenic DI can occur as a familial disorder or acquired during life. A number of familial varieties have been described, inherited as either an autosomal dominant or recessive trait. The majority of cases of neurogenic DI are due to acquired diseases (Table 1)
**TABLE I**

*CAUSES OF CENTRAL DIABETES INSIPIDUS*

I. Familial

II. Acquired

A. Idiopathic (30% have AVP neuronal antibodies)

B. Tumors of the brain

C. Head trauma

D. Granulomatous disease involving hypothalamic-pituitary area

E. CNS infections

F. Cerebral vascular disorders

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**Clinical presentation:** The clinical presentation of DI is limited to polyuria, polydipsia and thirst. Nocturia (excessive urination at night) is usually present and results in chronic tiredness, poor school or work performance, and malaise. In children, the presenting symptom may be enuresis. In secondary forms, the symptoms of the underlying disease also may be present. If DI is associated with anterior pituitary insufficiency, polyuria may not be manifest until the corticosteroid deficiency is corrected (due to the effect of cortisol in increasing free water clearance and increasing the threshold for AVP secretion). As long as fluid intake is sufficient to match urinary losses, physical examination is unremarkable. Clinical signs of dehydration may, however, develop if drinking is diminished owing to loss of thirst or to inability to obtain water because of neurologic or external impairments.

**Pathophysiology of polyuria:** Three pathogenic mechanism account for polyuria: 1) insufficient osmoregulated AVP, known as neurogenic DI, (2) complete or partial renal resistance to the antidiuretic action of AVP, known as nephrogenic DI, and (3) habitual fluid drinking or primary polydipsia. The nephrogenic form can occur as an idiopathic X-linked familial disease, mutation of the vasopressin V2 receptor gene, or may be due to various toxic, metabolic or other injuries to the kidney. Primary polydipsia is associated either with psychiatric illness (psychogenic DI) or with an abnormality in the thirst mechanism of idiopathic or specific etiology (dipsogenic DI).

**Investigation of polyuria:** Since there are no clinical features that definitely identify the cause of polyuria in a particular patient, diagnosis must rest on the results of endocrine investigations. Polyuria is defined by a urine volume greater than 2.5 liters per 24 hours. Patients with severe neurogenic DI, because of defective AVP secretion, have a random plasma osmolality which is in the high normal range and a random urine osmolality which is low (generally <300 mOsm/kg). After dehydration (water deprivation) their plasma osmolality will increase significantly (>295 mOsm/kg) while their urine remains dilute. After administration of AVP their renal tubules will respond and their urine osmolality will increase to over 750 mOsm/kg.
These patients’ plasma AVP level is low and does not increase normally by infusion of hypertonic saline solution.

Patients with severe nephrogenic DI also have random plasma osmolality in the high normal range and low urine osmolality. They also fail to respond to water deprivation, that is, their urine osmolality remains low and their serum osmolality will increase to a very high level. However, in contrast to patients with neurogenic DI, these patients do not respond to administration of AVP, (i.e., their urine osmolality remains low) and in response to hypertonic saline infusion they are able to increase their plasma AVP level.

Patients with primary polydipsia, because of excessive water drinking, have a low random plasma osmolality and a low urine osmolality. In contrast to the other groups, these patients respond to water deprivation by increasing their urine osmolality and maintain their serum osmolality within normal range (because they do not have a defect in AVP secretion or action). These patients respond to administration of AVP and increase their urine osmolality. However, if administration of AVP is after adequate water deprivation they are not able to increase urine osmolality any further because they have already increased their own AVP secretion in response to dehydration and saturated renal tubular cell AVP receptors. Patients with primary polydipsia will respond to hypertonic saline infusion and increase their plasma AVP level. (Table II).

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Differential Diagnosis of Polyuria

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<tr>
<th></th>
<th>Central Diabetes Insipidus</th>
<th>Nephrogenic Diabetes Insipidus</th>
<th>Primary Polydipsia</th>
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<tr>
<td>Random plasma osmolality</td>
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<tr>
<td>Random urine osmolality</td>
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<td>Urine osmolality during</td>
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<tr>
<td>mild water deprivation</td>
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<tr>
<td>Urine osmolality following AVP administration</td>
<td>No change</td>
<td>No change</td>
<td>↑</td>
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<td>(a) without water deprivation</td>
<td>↑</td>
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<tr>
<td>(b) after water deprivation</td>
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Plasma AVP after hypertonic saline infusion

|                          | No change | ↑ | ↑ |
EXCESSIVE SECRETION OF VASOPRESSIN

Several clinical conditions have been associated with inappropriately elevated levels of AVP. These conditions include congestive heart failure, cirrhosis of the liver and the syndrome of inappropriate secretion of antidiuretic hormone. The latter is discussed in detail in the following section.

**Syndrome of Inappropriate secretion of Anti-Diuretic Hormone (SIADH)**

A number of diseases are associated with plasma vasopressin concentration that is inappropriately high for that plasma osmolality. Thus, with normal water intake, there is water retention, leading to hyponatremia and hypo-osmolality.

**Etiology and pathophysiology:** The various causes of SIADH operate through three pathophysiological mechanisms (Table III).

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**TABLE III**

**CAUSES OF SIADH**

1. Malignant tumors with autonomous AVP release; e.g., carcinoma of the lung
2. Nonmalignant pulmonary diseases; e.g., tuberculosis
3. Central nervous system disorders; e.g., meningitis
4. Drugs- e.g., narcotics

In malignant tumors, AVP is synthesized, stored and autonomously released from tumor tissue in amounts that are determined largely by the tumor mass and not by known stimuli. Small-cell or oat-cell carcinoma of the lung accounts for 80% of such patients.

In the second type of SIADH, nontumorous lung tissue either acquires the capacity to synthesize and release AVP autonomously or reduces left atrial filling which stimulates central AVP release. This type of hyponatremia is a common feature of pulmonary tuberculosis and pneumonia.
The third type of SIADH involves release of AVP from the patient's neurohypophysis due to neighboring inflammatory, neoplastic, or vascular lesions (Group 3, Table III) or of drugs (Group 4, Table III), and independently of the normal stimuli.

The excessive AVP release in this syndrome, in the presence of normal water intake, results in water retention, hyponatremia, and extra- and intracellular hypotonicity. Sodium secretion is enhanced because of increased glomerular filtration rate and, probably, suppression of aldosterone secretion. In addition, atrial natriuretic hormone is released by volume expansion and contributes to the sodium loss. These urinary losses, which may be profound, aggravate the hypotonicity of body fluids, and, at the same time, prevent the development of edema or hypertension. This combination of factors leads to what many authors describe as a state of euvolemic hyponatremia (in contrast with the states of hypovolemic and hypervolemic hyponatremia).

Recently, hyponatremia (and a form of SIADH) due to rare activating mutations of the vasopressin V2 receptor gene in renal tubules has been reported.

**Clinical and laboratory features:** Patients with SIADH may present with weight gain, weakness, lethargy and mental confusion, ultimately progressing to convulsions and coma. Laboratory features include low serum levels of BUN, creatinine, uric acid and albumin. The serum sodium concentration is generally less than 130 mEq per liter, and the plasma osmolality is below 270 mOsm/kg. the urine is inappropriately hypertonic for the degree of plasma osmolality. Urinary sodium concentrations is usually more than 20 mEq per liter.

**Diagnosis:** SIADH should be suspected in any patient with hyponatremia who excretes urine that is hypertonic relative to plasma. The finding that urinary sodium concentration is greater than 20 mEq per liter provides further support for the diagnosis. To make the diagnosis of SIADH it is essential to exclude (1) hypovolemic or depletional hyponatremia, especially due to adrenal insufficiency, salt-losing nephropathy, diarrhea and previous diuretic therapy; (2) hyperovlemic hyponatremia associated with edematous states (congestive heart failure, cirrhosis, nephrotic syndrome); (3) pseudohyponatremia (associated with severe hyperlipidemia, hyperproteinemia, or severe hyperglycemia). In some patients with chronic debilitating diseases (such as some malignancies) the osmoreceptors are thought to "reset" at a subnormal level. Thus, AVP is released at levels of plasma osmolality below the normal osmotic threshold. This condition is called sick-cell syndrome or essential hyponatremia.

**Approach to Management.** Although detailed consideration of treatment is beyond the scope of the Endocrine Pathophysiology Module, the approach to management of SIADH includes

1) Treatment directed at the underlying disorder or withdrawal of offending drug (if clinically possible)

2) Water restriction to no more than 1000 ml/24 hours (most preferred)

3) Medications that block the effect of AVP on the distal and convoluted tubules of the kidney (e.g., demeclocycline or lithium). Lithium has numerous adverse effects, and demeclocycline must be used with caution in patients with hepatic dysfunction

4) Very careful infusion of hypertonic saline (risk of osmotic demyelination syndrome)

5) “Vaptans”: The three AVP receptor subtypes (V1a, V1b, and V2) are members of the rhodopsin-like G-protein-coupled receptor family. Several non-peptide AVP V2 receptor antagonists (known as vasopressin receptor antagonists [VRAs] or ‘vaptans’ have been
developed and are being studied for treating hyponatremia, fluid overload and other medical conditions. Relcovaptan, selective V1a-receptor antagonist, has shown promise in the treatment of Raynaud's disease and dysmenorrhea. The V2-receptor antagonists--mozavaptan, lixivaptan, satavaptan, and tolvaptan--induce a highly hypotonic diuresis without altering the excretion of electrolytes. These drugs thus are effective in the treatment of euvoalaemic and hypervolaemic hyponatraemia. Conivaptan is a V1a/V2 non-selective vasopressin-receptor antagonist that is FDA-approved as an intravenous infusion for the inpatient treatment of hyponatraemia. When administered to patients with SIADH and other water overload states, the vaptans promote pure water loss (aquaresis) without electrolyte wastage. This is in contrast to typical diuretics that induce natriuresis and kaliuresis.

**OXYTOCIN**

**Parturition and Lactation**
The primary stimuli for oxytocin release are mechanical distention of the reproductive tract (vagina) and suckling of the nipples; both act through neural pathways to effect oxytocin release. The cardinal actions of oxytocin are stimulation of uterine contractions at parturition and augmentation of intramammary pressure during suckling. Pharmacological doses of oxytocin, such as those employed for pregnancy termination and for induction of labor, can alter the metabolism of water by the kidney. One unit of oxytocin has about 0.01 units of antidiuretic activity due to its biochemical similarity to ADH and its action on the renal distal tubular receptors. Severe water intoxication has been reported in women infused with oxytocin at high rates and simultaneously given hypotonic fluids.

**Behavioral connection**
Since the discovery of its uterine-contracting properties in 1906 and subsequent description of its nonapeptide sequence, oxytocin research has focused almost exclusively on its peripheral roles in reproduction. Over the past few decades, studies have shifted to oxytocin’s effects in the mammalian brain. In addition to its localization within the magnocellular neurons of the hypothalamic paraventricular and supraoptic nuclei, smaller cells scattered around various parts of the brain provide the oxytocin locally for the modulation of various behaviors. To date, oxytocin has been associated with a variety of "non-social" behaviors, such as learning, anxiety, feeding and pain perception. Furthermore, emerging lines of evidence indicate that oxytocin might play important roles in modulating social memory, attachment, sexual and maternal behavior, aggression, human bonding, and trust. Based on this new expanded understanding, it has been hypothesized that oxytocin might be involved in the etiology of certain human disorders characterized by aberrant social interactions, such as autism and schizophrenia. Indeed, as argued by Lee et al (2009), most of the myriad functions attributed to oxytocin, including social interactions (affiliation, aggression), sexual behavior, parturition, lactation and maternal bonding, are teleologically consistent with facilitation of survival and propagation of the species.

References:


Plasma Osmolality = \(2 \times \text{Na}^+ \text{ (in mEq/L)} + \frac{\text{Glucose (in mg/dL)}}{18} + \frac{\text{BUN (in mg/dL)}}{2.8}\)
HYponatremia
Pathophysiology

Hypervolemic
Decreased effective blood volume
1. Retention of Na\(^+\) and water
2. Contributing factor ↑ADH

Hypovolemic
Decreased total body Na\(^+\)
Same pathophysiology
(Reduction in actual as well as effective blood volume)

Euvolemic (SIADH)
↑ADH
Expansion of body fluids
Dilational hyponatremia
↑ANP
(Essential or sick cell syndrome)

Clinical Presentation and Diagnosis

Hypervolemic
1. Edema
2. Signs of decreased effective blood volume

Hypovolemic
1. No edema
2. Signs of volume depletion

Euvolemic
1. Neurologic signs
2. No edema
3. No signs of volume depletion
4. No renal, adrenal, and thyroid deficiency

Laboratory Tests

Hypervolemic
BUN and plasma uric acid: increased
Plasma renin activity: increased
Urine [Na\(^+\)]: low, <20 mEq/L

Hypovolemic
BUN and plasma uric acid: increased
P.R.A.: increased
Urine [Na\(^+\)]: low, <20 mEq/L

Euvolemic
BUN and uric acid: low
P.R.A.: Low
Urine [Na\(^+\)]: high >20 mEq/L
Urine osmolality >100 mosmol/kg (inappropriately concentrated)
CASE PRESENTATION

Hyponatremia and weight loss in a 59-year-old man:

History: A 59-year-old steel mill worker is brought to the emergency room because of mental confusion. For about six months his family has noticed that his appetite has been poor and that his weight has decreased about 35 pounds. He has smoked 1 pack per day for the past 30 years. He complains of excessive fatigue, muscle weakness and a chronic, nonproductive cough. About two weeks ago he was noted to be unusually irritable, and two days ago he became irrational, confused and disoriented. He ordinarily drinks about six bottles of beer and smokes two packs of cigarettes per day. The remainder of his history is unremarkable.

Examination: He is a disoriented, irritable, chronically ill man, who has obvious signs of weight loss. His blood pressure of 140/80 mmHg, supine, does not change with standing. His pulse is 100/minute, respirations 18/minute, and temperature 101°F. Funduscopy and visual fields are normal. The cardiovascular exam is normal. Chest exam discloses hyper-resonance and bilateral bronchovesicular breath sounds with persistent wheezing in the right upper lung field. There is a hard 3 x 2 cm. lymph node palpable in the left supraclavicular fossa. The liver is palpable 4 cm below the right costal margin, and is firm, smooth and estimated to be 17 cm in the midclavicular line. Extremities show early clubbing of the fingernails, but no edema is detected. Except for confusion, bilaterally decreased deep tendon reflexes, and extensor toe reflexes, the neurologic exam is unremarkable. CT scan of the chest showed a mass lesion in the upper lobe of the right lung.

Laboratory data:

Hb 9.0% 01, 14-18)
Hct 26% (nl, 42-52%)
WBC 14,946/mm3 (nl, 4,800-10,800)
  PMN's 92% (nl, 50-70%)
  lymphocytes 8% (nl, 20-40%)
Plasma cortisol
  8:00 a.m. 25 µg/dl (nl, 5-25)
  8:00 p.m. 10 µg/dl (nl, 3-10)
Serum (not lipemic)
  Glucose (fasting) 90 mg% (nl, 71-115)
  Urea nitrogen 8 mg% (nl, 4-18)
  Creatinine 0.9 mg% (nl, 0.7-1.3)
  Na 115 mEq/L (nl, 137-145)
  K 3.8 mEq/L (nl, 3.5-5.0)
  Cl 80 mEq/L (nl, 96-108)
  CO2 24 mEq/L (nl, 24-32)
  Ca 9.2 mg% (nl, 8.5-10.4)
  Phos.3.1 mgT (nl, 2.3-4.6)
  Protein 6.1 mg% (nl, 6.0-8.0)
  Bilirubin 1.1 mg% (nl, 0.1 - 1.1)
  Alk phos 3 units (nl, 1-4)
  SGOT (ALT) 21 units (nl, 12-40)
Urinalysis
  sp gr 1.024 (nl, 1.003-1.035)
  pH 6.8 (nl, 5-9)
  glucose - negative
  ketones - negative
  protein - negative
  microscopic - negative
Urine:
  NaCl 6 gm/day
X-rays
  chest - To be shown
  skull - normal
EKG - nonspecific ST-T wave changes
Serum osmolality 235 mOsm/kg (278-305)
Urine osmolality 410 mOsm/kg (300-900)
osmolalities performed simultaneously
The following questions will be discussed during the lecture:

1. The severe hyponatremia seen in this man can most likely be attributed to:
   (Choose one only)
   
   A. Oat cell carcinoma of the lung with cerebral metastases
   C. Oat cell carcinoma of the lung with hypothalamic-pituitary metastases
   D. Oat cell carcinoma of the lung with paraneoplastic secretion of ADH
   E. Malnutrition and salt depletion due to renal salt wasting

2. The urine concentration in this patient is: (Choose one only)
   
   A. Inappropriately dilute
   B. Appropriately dilute when the serum osmolality is taken into consideration
   C. Inappropriately concentrated
   D. Appropriately concentrated when the serum osmolality is taken into consideration

3. Which of the following measures would be expected to increase serum sodium level in this patient? (True or False)
   
   A. Infusion of 0.9% (normal) sodium chloride solution
   B. Restriction of fluid intake to 1000 ml/day
   C. Infusion of 5% dextrose in water
   D. Administration of conivaptan (vasopressin V2 receptor antagonist)
   E. Infusion of 3% hypertonic sodium chloride solution
   F. Treatment with the antibiotic demeclocycline