NELSON Textbook of Pediatrics

FOURTEENTH EDITION

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blood salicylate level depends in part on the interval between the time the drug was ingested and the time the blood sample was obtained; a level of 35 mg/dL 36 hr after an acute ingestion or after the start of aspirin therapy may be more significant than a level of 60 mg/dL 2 hr after acute ingestion when peak levels may be expected. Figure 6–10 can help determine the severity of an acute overdose, given the serum salicylate level and the time since ingestion.

In chronic ingestion it should be remembered that even though a salicylate level of 35 mg/dL may be required to obtain therapeutic benefits in older children, fatal cases of salicylism have occurred in infants with lower blood levels; the need for active treatment depends only in part on blood levels of salicylate and on whether the overdose is acute or chronic. Clinical factors are equally important. Coma, convulsions, marked hyperventilation, oliguria, respiratory depression, severe azotemia, or marked reduction in the plasma level of bicarbonate or P_{CO_2} indicates the need for active therapeutic intervention.

Treatment is designed to prevent further absorption of salicylate, to correct deficits and replace ongoing losses of fluids and electrolytes (which are increased above normal), and to reduce tissue levels of salicylate by facilitating excretion of the drug.

The efficacy of attempting to empty the gastrointestinal tract of salicylate is controversial. However, in the absence of central nervous system depression, gastric emptying can be attempted for up to 10 hr following ingestion of the salicylate. Syrup of ipecac (dose in children over 1 yr of age: 1 tbsp [15 mL] repeated after 20 min if vomiting does not occur) is probably still the most effective emetic, and a slurry of activated charcoal can be given later in an attempt to prevent further absorption of any remaining salicylate from the bowel.

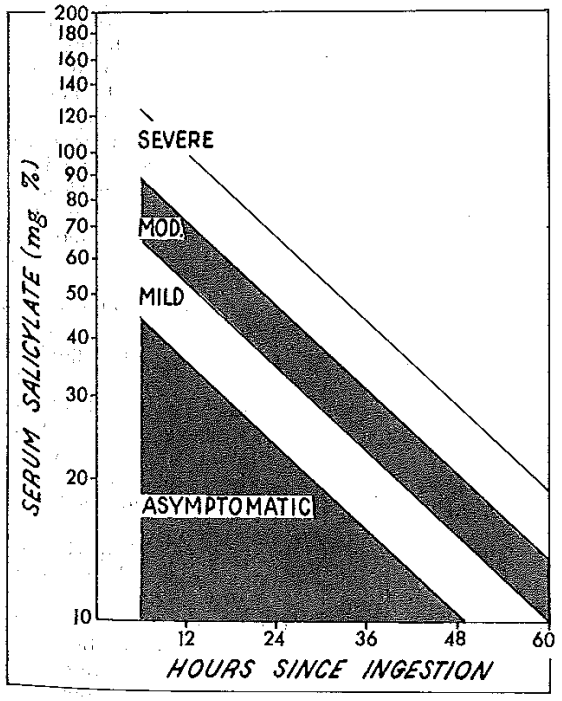

Figure 6–10. Nomogram relating serum salicylate concentration and expected severity of intoxication at varying intervals following the ingestion of a single dose of salicylate. (From Done AK: Salicylate intoxication: Significance of measurements of salicylate in blood in cases of acute ingestion. Pediatrics 26:800, 1960. Copyright 1960. Reproduced by permission of Pediatrics.)

If the patient is in shock, an isonatremic solution is indicated to expand plasma volume; otherwise, a hyponatremic solution can be used to replace fluid and electrolyte deficits.

The amount of fluid required ranges in individual patients from 2,000 to 5,500 mL/m²/24 hr. This fluid should contain sodium, 40–50 mEq/L, some of which should be sodium bicarbonate and, if there is adequate renal function, potassium, to 40 mEq/L. Oral potassium salts may be used to supplement the intravenous therapy. Administering carbohydrate appears to improve prognosis; intravenous fluids should contain at least 5% glucose.

Treatment is designed to replace maintenance losses of fluids and electrolytes, which may be twice normal because of increased evaporative losses, to replace deficits, and to maintain a diuresis to facilitate excretion of salicylate. A urine volume of at least 2,000 mL/m²/24 hr with a specific gravity of less than 1.010 is a reasonable goal. The early administration of sodium bicarbonate to maintain an alkaline urine (pH higher than 7.5) facilitates excretion of salicylate by reducing its back-diffusion in ionized form from tubular urine through the lipid membranes of the renal tubular cells; the clearance of salicylate with a urine pH greater than 8.0 is 20 times that at a urine pH of 6.0. The dose of bicarbonate necessary to alkalinize the urine is approximately 2 mEq/kg, given over 1 hr. An additional 2 mEq/kg of sodium bicarbonate should be given if the urine pH does not reach 7.0. The urinary pH should then be checked every 30 min. If the pH falls below 7.0, additional sodium bicarbonate should be given with appropriate amounts of potassium to avoid renal tubular potassium depletion and paradoxic aciduria.

Acetazolamide (5 mg/kg repeated 2 or 3 times in 24 hr) also increases salicylate excretion; this therapy has not received general acceptance because of reported complications, including seizures, and an increased mortality in experimental animals. Peritoneal dialysis or hemodialysis should be considered for severely ill patients as a means for removing additional amounts of salicylate loosely bound to plasma proteins. Such patients include those with blood levels of salicylate above 100 mg/dL, those with an elevated P_{CO_2}, those with severe acidosis, or those who have failed to respond adequately to alkalinization. The efficiency of dialysis is increased by the addition of albumin to the dialysis fluid. Exchange transfusion is a relatively inefficient means of removing salicylate in the critically ill patient. If done, heparinized blood should be used because of the often lethal exacerbation of acidosis if citrated blood is used.

Vitamin K_1 oxide (Konakion) should be given intramuscularly to offset possible prothrombin deficiency.

6.24 ELECTROLYTE DISTURBANCES ASSOCIATED WITH CENTRAL NERVOUS SYSTEM DISORDERS

Diseases of the central nervous system are frequently associated with disturbances in sodium concentration. Three types of changes have been described:

1. Patients with diverse lesions, such as surgical or traumatic damage to the brain, encephalitis, bulbar poliomyelitis, cerebrovascular accidents, tumors of the 4th ventricle, and subdural hematomas, may lose large amounts of sodium in the urine. Dehydration, hypotension, and azotemia result unless large amounts of salt are administered and the intake of water is limited.

2. Patients with tuberculous meningitis who are severely ill and comatose are frequently hyponatremic but exhibit no symptoms that can be attributed to hyponatremia. This situation may be analogous to the asymptomatic hyponatremia of severe malnutrition or pulmonary disease. Relatively large

amounts of salt may be lost in the urine when attempts are made to correct the hyponatremia by salt loading. Careful clinical and laboratory observations are essential to ensure that salt depletion and water intoxication do not occur. Potassium should be administered in amounts at least 50% greater than with usual maintenance therapy.

3. Patients with acute infections of the central nervous system occasionally have symptoms of acute water intoxication, with a rapid fall in the serum sodium level. These patients retain an excessive amount of water and have increased thirst. Convulsions are severe and resistant to drug therapy but respond to the intravenous administration of hypertonic saline solution and subsequent restriction of fluid.

These disorders may result from lesions involving the thirst center, osmoreceptors, or supraopticohypophyseal tract, from inappropriate secretion of ADH, or from other lesions.

Convulsions or other symptoms from cerebral edema may respond to hypertonic mannitol solution, although care in its administration should be taken in patients with impaired renal function.

6.25 PREOPERATIVE, INTRAOPERATIVE, AND POSTOPERATIVE FLUIDS

See Sec. 6.48–6.52.

Preoperatively preparing a patient having no pre-existing deficit or in whom the deficit has been repaired consists mainly of supplying carbohydrate to ensure adequate storage of glycogen in the liver. Usual maintenance requirements of water and electrolytes are appropriate. Young infants who are not vomiting should receive carbohydrate and sodium chloride mixtures by mouth until 3 hr before operation. Such fluids are readily absorbed from the gastrointestinal tract and do not produce aspiration pneumonitis if vomited and aspirated.

Preoperatively preparing the newborn involves certain unique hazards. Deficits of water and electrolytes from vomiting or from stasis caused by intestinal obstruction should be replaced before operating. If aspiration pneumonitis is suspected, it should be treated with antibiotics. Nasogastric suction may be inadequate. If so, *gastrostomy* should be performed to aid in decompression and in postoperative feeding. In intestinal obstruction conjugated bilirubin may be deglucuronidated by intestinal enzymes; an enterohepatic circulation of unconjugated bilirubin can then lead to high serum levels and kernicterus. Hypoprothrombinemia should be prevented by administering 1 mg of vitamin K_1 oxide.

The most common error in administering parenteral fluid during and after surgery is overadministration, particularly of dextrose in water. Table 6–17 lists maintenance water requirements during surgery. Additional amounts of blood, plasma, saline, or other volume expander must be given if blood loss or tissue trauma is significant. The magnitude of such losses is best judged by the experienced surgeon as he or she operates.

Under most circumstances no potassium should be administered during this time, because extensive tissue trauma or anoxia may result in the release of large amounts of intracellular potassium with the potential of causing hyperkalemia. Moreover, if shock occurs, it may be complicated by acute renal failure, making treatment of the hyperkalemia more difficult.

Postoperatively, intake should be limited for 24 hr. Thereafter, usual maintenance therapy is gradually resumed. The water intake should not exceed 85 mL/100 kcal metabolized because of antidiuresis resulting from trauma or circulatory readjustment unless renal ability to concentrate the urine is limited (e.g., in sickle cell anemia). If the intake of water is not limited, whether given parenterally or by mouth, water intoxication may result. Maintenance sodium intake should also be low because of the low caloric expenditure during anesthesia and postoperatively.

Some postoperative children have elevated blood ADH levels but not the inappropriate ADH syndrome. Rather, the ADH release is an appropriate response to very severe fluid restriction with resultant volume contraction.

6.26 ISOLATED DISTURBANCES IN CONCENTRATIONS OF ELECTROLYTES

ACIDOSIS. *Respiratory acidosis,* in which the pH may be markedly lowered, primarily as a result of retention of carbon dioxide, may be seen with severe respiratory insufficiency, with respiratory distress syndrome in the newborn infant, and in patients receiving assisted ventilation for any reason. Mild metabolic acidosis may also exist because hypoxia leads to the accumulation of lactic and other organic acids in the extracellular fluid. Measurements of blood pH and gases should guide correction of acidosis. The appropriate treatment is to improve ventilation by assisting respiration rather than by administering sodium bicarbonate, which may produce hyperosmolality and cardiac failure.

Metabolic acidosis, resulting, for example, from renal tubular acidosis or from accumulation of organic acids, may require the administration of alkali, especially if symptoms are evident. In lactic acidosis, in glycogen disorders, or in circulatory insufficiency and hypoxia, sodium lactate may not be adequately metabolized; in these situations sodium bicarbonate is the preferred agent. The usual initial dose is 1–2 mEq/kg. However, a more precise estimate of the dosage required is given by the general formula

$$(C_d - C_a) \times f_d \times \text{body weight [in kg]} = \text{mEq required}$$

where C_d and C_a represent, respectively, the serum bicarbonate concentration desired and the one actually present, expressed as mEq/L; and f_d represents that fraction of the total body weight in which the administered material is apparently (not actually) distributed (the value for f_d varies with the substance administered). The f_d for bicarbonate or potential bicarbonate approximates 0.5–0.6. Such calculations indicate that 0.5 mL/kg of a molar solution of sodium bicarbonate would raise the serum bicarbonate concentration approximately 1 mEq/L. However, responses to administered bicarbonate vary widely, because it may be sequestered in bone or muscle or lost in urine.

With glomerular insufficiency, acidosis should be corrected cautiously, because the sodium administered with bicarbonate may result in further expansion of the extracellular fluid volume. It is rarely necessary to attempt to increase serum bicarbonate levels above 15 mEq/L unless the patient continues to be markedly symptomatic from the acidosis. Overcorrecting acidosis also may be complicated by tetany. If hyperphosphatemia coexists with acidosis, it should be treated simultaneously with low-phosphate diets and oral calcium carbonate.

Treating with sodium bicarbonate should always be considered a temporizing measure; every attempt should be made to treat the underlying cause, such as using glucose and insulin in diabetic ketoacidosis, improving circulation in shock, or eliminating salicylates, methanol, or other toxins.

Severe metabolic acidosis is an integral part of *cardiovascular shock.* Relying on arterial blood gas values to monitor treatment in patients in shock and receiving mechanical ventilation is misleading. There is an exaggerated difference between arterial and central venous values for pH and P_{CO_2} in this situation, necessitating additional sampling of venous blood through a central venous line (see Sec. 6.34).

TABLE 6–17. Approximate Requirements of Water Without Electrolytes During Operation*

Weight (kg)	Basal (kcal/24 hr)	Evap. Water, mL/hr (90 mL/100 kcal/24 hr)†	Urine Water, mL/hr (30 mL/100 kcal/24 hr)‡	Total (mL/hr)§
3	150	6	2	8
5	270	10	3	13
7	410	15	5	20
10	550	21	7	28
20	850	32	10	42
30	1,100	41	14	55
40	1,300	49	16	65

*From Harned HS Jr, Cooke RE: Surg Gynecol Obstet 104:543, 1957. By permission of Surgery, Gynecology & Obstetrics.
†This value is assumed to be high because of possible sweating and hyperventilation.
‡This value is assumed to be low because of probable antidiuresis.
§This does not include abnormal losses of fluid (hemorrhage, wound edema, suction) that must be replaced by appropriate electrolyte-containing fluids.

ALKALOSIS. Normally, the kidney has an enormous capacity to excrete bicarbonate, and increased amounts of blood bicarbonate are promptly excreted. However, under certain circumstances, *metabolic alkalosis* may develop and be maintained. Typically, it is caused by the administration of excess amounts of alkali, by the loss of hydrogen ion, or by volume contraction with disproportionate losses of chloride. Severe hypokalemia can result in alkalosis, too, or may perpetuate it.

The plasma bicarbonate level is elevated and respiratory compensation results in hypoventilation and an increase in P_{CO_2}. Rarely, respiration may be so depressed in infants with severe hypochloremic alkalosis that blood oxygenation is diminished. Severe alkalotic tetany may also occur. In such instances, administering ammonium chloride may effect symptomatic improvement; the dose may be calculated from the general formula presented above, with the probable f_a being 0.2–0.3. Such therapy only relieves symptoms and should not be used in place of correcting the contracted volume of body fluids or administering potassium chloride to repair intracellular deficits.

Metabolic alkalosis associated with volume contraction responds to measures designed to expand volume and replace the chloride and potassium deficits. It occurs in patients with acid-base disorders caused by vomiting, gastric suction, congenital chloride diarrhea, dietary chloride deficiency, or administration of diuretics. Their urinary chloride concentration is low (10 mM/L or less). A minority of patients are "chloride-resistant," with urinary chloride concentrations of 15 mM/L or greater because of hyperadrenalism, Bartter syndrome, severe potassium depletion, or licorice ingestion. Potassium repletion, using potassium chloride and not potassium phosphate, as well as specific therapy directed to the underlying condition, is indicated.

Respiratory alkalosis occurs in salicylate intoxication, in various central nervous system diseases such as trauma, infection, or tumors, with anxiety or fever, and in congestive heart failure, hepatic insufficiency, and gram-negative septicemia. Treatment should be directed at removing the underlying cause, although measures designed to return the P_{CO_2} to normal may be indicated. Acidifying agents such as ammonium chloride are not indicated.

HYPONATREMIA. The serum sodium level is most commonly reduced as a result of either sodium depletion or water "intoxication" or a combination of both (Table 6–18). A low serum sodium level, thought to be a result of redistribution of total body sodium, may also occur in association with severe illnesses or in the terminally ill patient. In addition, *apparent* hyponatremia may be observed as an artifact, such as in diabetic ketoacidosis when the water content of plasma is reduced by the presence of increased quantities of lipids. This error is avoided by laboratory methods that determine sodium activity rather than concentration.

Patients with a serum sodium below 120 mEq/L are usually symptomatic (e.g., convulsions, shock); those with lesser degrees of hyponatremia are frequently asymptomatic. Treatment of *asymptomatic hyponatremia* depends on its cause. With water overload, fluid restriction is the appropriate measure; the serum sodium level may return rapidly to normal if there is good renal function but may take several days or weeks with the inappropriate ADH syndrome. When sodium deficits are present, adding extra salt to the diet or increasing the

TABLE 6–18. Clinical States Complicated by Hyponatremia

- Expansion of extracellular space by water
  - Excessive intake
    - Parenteral fluid therapy—glucose in water
    - Oral (with diminished output)
    - Tap water enemas
    - Allergy to cow's milk (very rare)
  - Diminished output (usual intake)
    - Renal
      - Intrinsic: nephritis, nephrotic syndrome, tubular necrosis, prematurity
      - Extrinsic
        - Excess of antidiuretic hormone: acute and chronic central nervous system disease, vasopressin therapy, surgery, pulmonary disease
        - Circulatory: heart failure, cardiovascular surgery, malnutrition
    - Skin: premature infant in very humid environment
- Deficiency of extracellular sodium
  - Inadequate intake
    - Low-salt diet
    - Parenteral therapy with glucose in water
  - Excessive losses
    - Gastrointestinal: vomiting, salivary, gastric, biliary, pancreatic drainage, diarrhea, resin therapy, tap water enemas (especially in megacolon)
    - Genitourinary
      - Intrinsic renal disease: chronic nephritis, acute tubular necrosis (recovery phase), nephrotic syndrome (diuresis)
      - Extrinsic influences: diuretics, acetazolamide, hypoadrenalism, central nervous system disease (rare), expanded volume (Pitressin, excessive water therapy)
    - Skin
      - Normal sweat
      - Abnormal sweat: cystic fibrosis, adrenal insufficiency
      - Burn therapy with silver nitrate (hypochloremia)
    - Cerebrospinal fluid
      - Draining myelomeningocele
      - Arachnoureterostomy
      - Continuous drainage of cerebrospinal fluid (e.g., in lead encephalopathy)
    - Parenteral: thoracentesis, paracentesis, burns
  - Redistribution
    - Severe malnutrition
    - Potassium deficiency
    - Trauma

sodium concentration of parenterally administered fluid often corrects the deficit. Measuring urine sodium concentration helps determine the cause of hyponatremia. Typically, with sodium depletion, urine sodium concentration is 10 mEq/L or less, although such low values are also found in nephrotic syndrome, congestive heart failure, or hepatic failure. Expansion of the extracellular fluid with water or renal tubular injury results in a higher urinary sodium concentration (around 50 mEq/L). The wrong treatment does not correct the defect and may be detrimental. For example, administering sodium to a patient with hyponatremia resulting from water excess, such as that seen with the chronic edema of heart failure, nephrotic syndrome, or cirrhosis, may result only in further expanding the extracellular fluid without correcting the serum sodium level.

Treatment of *symptomatic hyponatremia* consists of administering a hypertonic saline solution, calculated according to the formula in the preceding section on acidosis, with C representing serum sodium rather than bicarbonate. Because there is osmotic equilibrium between cells and extracellular water, changes in osmolality are distributed over total body water so that the value for f_d should be 0.6–0.7. A dose of 12 mL/kg of body weight of 3% sodium chloride solution (6 mEq sodium/kg) usually raises the serum sodium level by approximately 10 mEq/L. Correction of hyponatremia may be associated with myelinolysis in the central nervous system. Therefore, the initial rapid therapeutic increase in the serum sodium level should only be to a value of about 125 mEq/L. Subsequent elevation of the sodium concentration should be effected in small increments (5–10 mEq/L) over 1–4 hr. Hypernatremia should be avoided.

HYPERNATREMIA. This may result from faulty preparation of infant formulas: using condensed instead of evaporated milk or using heaped or packed instead of level measures of milk powder. These errors increase the solute load to be excreted by the kidney relative to the amount of water provided and may result in an osmotic diuresis and negative water balance. The accidental ingestion of excessive amounts of sodium chloride (*salt poisoning*) may also result in hypernatremia with serious residuals. The accidental substitution of salt for cane sugar in private homes and institutions occurs with sufficient frequency to justify the routine use of liquid sugars in infant feeding. The excessive intake of sodium is accompanied by increases in total body sodium and in the volume of extracellular water. Severe acidosis results from a shift of organic acids and free hydrogen ions to extracellular fluid. With shift of water from brain cells distention of cerebral vessels occurs, leading to subdural, subarachnoid, and intracerebral hemorrhage. The complications and residuals of salt poisoning are similar to, but may be more severe than, those seen with hypernatremic dehydration.

Hypernatremia is still associated with a high mortality rate, especially if the serum sodium concentration exceeds 158 mEq/L. Treatment is directed toward the rapid removal of excess sodium from the body. Intravenous fluids should consist of glucose in water, potassium acetate, and calcium, as needed. *Intermittent peritoneal dialysis* with glucose solutions can remove large quantities of sodium, correcting the hyperosmolality without the danger of pulmonary edema and heart failure. Approximately 45 mL/kg of a commercial dialysis solution containing 4.25% glucose can be injected intraperitoneally for severe hypernatremia (serum sodium concentration more than 200 mEq/L) and withdrawn 1 hr later. As the concentration of sodium in the serum falls, subsequent dialysis may be carried out using a solution with 1.5% glucose so as not to remove too much water and dehydrate the patient. Exchange transfusion is not a substitute for dialysis, because enormous quantities of blood would be required to effect a change in osmolality of total body water. Phenobarbital should be administered to prevent or control seizures. Digitalization may be necessary to counteract heart failure.

The treatment of hypernatremic dehydration is discussed in Sec. 6.18.

HYPOKALEMIA. Disturbances in the potassium concentration occurring without changes in volume of body fluids have been described in primary hyperaldosteronism and in Bartter syndrome. Large amounts of potassium are lost in the urine, resulting in low serum potassium and high serum bicarbonate concentrations. In congenital alkalosis of gastrointestinal origin, large amounts of potassium and chloride are lost in the stools. Using thiazide and loop diuretics (e.g., ethacrynic acid and furosemide) causes kaliuresis and natriuresis; prolonged use may result in significant potassium loss and hypokalemia.

Severe hypokalemia may result in weakness of skeletal muscles, decreased peristalsis, ileus, and an inability of the kidney to concentrate urine. Prolonged hypokalemia results in characteristic pathologic changes in the kidney and a decrease in function, which may persist even after potassium repletion.

Treatment consists of administration of large amounts of potassium (usually up to 3 mEq/kg/24 hr); in Bartter syndrome up to 10 mEq/kg may have to be given orally.

HYPERKALEMIA. Marked elevation of the serum potassium level results in ventricular fibrillation and death. Levels above 6.5 mEq/L should be treated promptly. The possibility of orally or parenterally administering excessive amounts of potassium should be considered and all potassium intake discontinued. The rapid intravenous administration of sodium bicarbonate (up to 2 mEq/kg over a 5- to 10-min period) or glucose and insulin (0.5 g of glucose/kg with 0.3 unit crystalline insulin/g of glucose, given over a 2-hr period) results in the intracellular movement of potassium and lowers the serum potassium level. Intravenous calcium gluconate (up to 0.5 mL of a 10% solution/kg given over 2–4 min) counters the cardiac toxicity of potassium, but the ECG should be monitored while it is being administered. None of these measures removes significant quantities of potassium from the patient; they are temporizing measures until negative potassium balance is established by the use of ion exchange resins (Kayexalate, 1 g/kg/24 hr, in divided oral doses twice daily or as a retention enema), by hemodialysis, or by peritoneal dialysis.

HYPOCALCEMIA AND HYPERCALCEMIA. These are discussed in Sec. 4.30, 6.27, 6.28, 9.54, and 19.17.

HYPOMAGNESEMIA. The importance of magnesium in intravenous therapy is reviewed in Sec. 6.7 and 6.29. The only definitive symptom complex associated with hypomagnesemia (serum magnesium level less than 1.3 mEq/L) is that of latent or manifest tetany. Convulsions, muscular twitching, disorientation, athetoid movements, carpopedal spasm, and hyper-reactivity to mechanical and auditory stimulation have been observed. Lowered serum concentrations and whole body deficits of magnesium are found in chronic diarrhea or vomiting, sprue, celiac disease, prolonged parenteral fluid therapy, and hyperaldosteronism. Low serum magnesium levels have been observed in infantile tetany, presumably on the basis of transient hypoparathyroidism. The intramuscular injection of 0.1 mL of a 24% solution of $MgSO_4 \cdot 7H_2O$ (0.2 mEq/kg) repeated every 6 hr for three or four doses produces symptomatic and biochemical improvement. Adding 3 mEq/L of magnesium to maintenance fluids for patients requiring long-term therapy may decrease the chance of serious deficiency (see Sec. 9.54).

HYPERMAGNESEMIA. Levels of serum magnesium higher than 10 mEq/L are accompanied by drowsiness and, occasionally, coma. Such levels rarely occur in the absence of renal failure. Deep tendon reflexes may also be abolished, and respiratory depression may occur at higher concentra-

appear to have an unexplained nocturnal deficiency of vasopressin secretion. The dose required is slightly higher (20–40 μg) than that used to treat neurogenic diabetes insipidus. It is given as a nasal spray before bedtime.

Nephrogenic Diabetes Insipidus
(Vasopressin-Insensitive Diabetes Insipidus)

See Sec. 18.30.

19.4 INAPPROPRIATE SECRETION OF ANTIDIURETIC HORMONE
(Hypersecretion of Vasopressin)

The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is now recognized as one of the most common aberrations of arginine vasopressin (AVP) secretion. In this condition plasma levels of AVP are inappropriately high for the concurrent osmolality of the blood and are not suppressed by further dilution of body fluids.

ETIOLOGY. The syndrome is being recognized in an increasing number of clinical conditions, particularly those involving the central nervous system, including meningitis, encephalitis, brain tumor and abscesses, subarachnoid hemorrhage, Guillain-Barré syndrome, head trauma, and after transsphenoidal surgery for pituitary tumors. Pneumonia, tuberculosis, acute intermittent porphyria, cystic fibrosis, infant botulism, perinatal asphyxia, use of positive-pressure respirators, and certain drugs such as vincristine and vinblastine also produce the syndrome. The mechanism of the disturbed regulation of vasopressin in these conditions is not fully understood, but in many instances there is direct involvement of the hypothalamus. The syndrome has been observed in patients with Ewing sarcoma; with malignant tumors of the pancreas, duodenum, or thymus; and particularly with oat cell carcinoma of the lung. In these instances the tumor presumably synthesizes and secretes vasopressin, the syndrome disappearing when the tumor is removed. In rare cases no cause for the syndrome has been found.

The syndrome has occurred during chlorpropamide therapy for diabetes mellitus, presumably because this drug potentiates vasopressin. Patients with diabetes insipidus treated with various antidiuretic preparations readily develop the syndrome during periods of excessive ingestion of fluids or during intravenous fluid therapy.

CLINICAL MANIFESTATIONS. The syndrome is probably most often latent and asymptomatic and forms the basis for the long known observation that serum sodium levels may be unexpectedly low in conditions such as pneumonia, tuberculosis, and meningitis. Careful attention to fluid replacement in patients with conditions known to be associated with the syndrome may prevent the development of symptoms.

The clinical manifestations are attributable to hypotonicity of body fluids and are those of water intoxication. If the serum sodium is not below 120 mEq/L, there may be no symptoms. Early, there is loss of appetite followed by nausea and sometimes vomiting. Irritability and personality changes, including hostility and confusion, may occur. When the serum sodium falls below 110 mEq/L, neurologic abnormalities or stupor is common, and convulsive seizures may occur. Skin turgor and blood pressure are normal, and there is no evidence of dehydration.

Serum sodium and chloride concentrations are low, whereas serum bicarbonate usually remains normal. Despite low serum sodium there is continued renal excretion of sodium. The serum is hypo-osmolar, but the urine is less than maximally dilute, and its osmolality is greater than appropriate for the tonicity of the serum. Hypouricemia is often present, probably owing to increased urate clearance secondary to volume expansion. Concurrence of hypouricemia with hyponatremia is a clue to the diagnosis of SIADH and is especially helpful in the neonate. Renal and adrenal functions are normal.

TREATMENT. Successful treatment of the underlying disorder (meningitis, pneumonia) is followed by spontaneous remission. Immediate management of the hyponatremia consists simply of *restriction of fluids*. Sodium should be made available to replace the soidum loss; hypertonic saline solution is usually of little benefit, however, since even large sodium loads are excreted in the urine. In cases of severe water intoxication, with convulsions or coma, administration of hypertonic saline solution will increase osmolality and control the central nervous system manifestations. In such emergencies administration of furosemide with 300 mL/m² of 1.5% sodium chloride will cause both a rise in sodium levels and a diuresis. Demeclocycline interferes with the action of AVP on the renal tubule. Experience in adults with SIADH indicates that this agent may be useful, but its role in the treatment of children is not established. An 8-yr-old child with chronic SIADH has been successfully treated with single daily doses of furosemide.

19.5 HYPERPITUITARISM

Hypersecretion of pituitary hormones is an expected finding in conditions in which deficiency of a target organ gives decreased hormonal feedback, as in primary hypogonadism or hypoadrenalism. In primary hypothyroidism pituitary hyperfunction and hyperplasia can enlarge and erode the sella and on rare occasions increase intracranial pressure. Such changes are not to be confused with primary pituitary tumors; they disappear when the underlying thyroid condition is treated. Pituitary hyperplasia also occurs in response to stimulation by ectopic production of releasing hormones such as that seen occasionally in patients with Cushing syndrome, secondary to CRH, or in children with acromegaly, which is secondary to GHRH produced by a variety of systemic tumors.

Primary hypersecretion of pituitary hormones by a suspected or proved adenoma is rare in childhood. The most commonly encountered pituitary tumors are those that secrete corticotropin, prolactin, or GH. With very rare exceptions, pituitary adenomas that secrete gonadotropins or thyrotropin occur primarily in adults. Hypothalamic hamartomas that secrete gonadotropin-releasing hormone are known to cause precocious puberty. It is suspected that some pituitary tumors may result from stimulation with hypothalamic-releasing hormones. Any pituitary tumor may also cause various hormonal deficiencies by compressing pituitary tissue.

Pituitary Gigantism and Acromegaly

In young persons with open epiphyses, overproduction of GH results in gigantism; in persons with closed epiphyses, the result is acromegaly. Often some acromegalic features are seen with gigantism, even in children and adolescents; after closure of the epiphyses, the acromegalic features become more prominent.

ETIOLOGY. Pituitary gigantism is rare. The cause is most often a pituitary adenoma, but gigantism has been observed in a 2.5-yr-old boy with a hypothalamic tumor that presumably secreted GHRH. Other tumors, particularly in the pancreas, have also produced acromegaly owing to secretion of large amounts of GHRH with resultant hyperplasia of the somatotrophs; GHRH was first isolated from two such pancreatic tumors. Growth hormone–secreting adenomas are also