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Debarati Bhar

CHAPTER 2

Endocrinology and Metabolism

Sattik Siddhanta

ADDISON'S DISEASE

Addison's disease or primary adrenal insufficiency is characterized by deficient production or action of glucocorticoids and/or mineralocorticoids and adrenal androgens.

CLINICAL FEATURES

- General malaise, fatigue, weakness, anorexia, weight loss, nausea, vomiting, abdominal pain or diarrhea, which may alternate with constipation, hypotension,
- Hyperpigmentation of skin and mucous membranes
- Hypotension
- Decreased axillary and pubic hair, and loss of libido and amenorrhea in women

INVESTIGATIONS

- **Metabolic acidosis**
- **Hyponatremia and hyperkalemia**
- **Basal morning serum cortisol and plasma adrenocorticotropic hormone (*ACTH*) concentrations:**

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Serum cortisol levels are highest in the early morning hours (06:00h–08:00h), ranging between 10–20 μg/dL. Serum cortisol concentrations determined at 08:00h of <3 μg/dL (80 nmol/L) are strongly suggestive of adrenal insufficiency while values below 10 μg/dL (275 nmol/L) make the diagnosis likely. Basal plasma ACTH concentration at 08:00h, when determined simultaneously with the measurement of basal serum cortisol concentration, may both confirm the diagnosis of adrenal insufficiency and establish the cause. The normal values of basal 08:00h plasma ACTH concentrations range between 20–52 pg/mL (4.5–12 pmol/L). In primary adrenal insufficiency, the 08:00h plasma ACTH concentration is elevated.

- **Basal plasma renin and aldosterone concentrations:** Primary adrenal insufficiency is associated with increased concentration or activity of plasma renin, low aldosterone concentrations, hyperkalemia and hyponatremia.
- **Standard dose ACTH stimulation test:** Adrenal insufficiency is usually diagnosed by the standard-dose ACTH test, which determines the ability of the adrenal glands to respond to 250 μg intravenous or intramuscular administration of ACTH by measurement of serum cortisol concentrations

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at 0, 30 and 60 min following stimulation. The test is defined as normal if peak cortisol concentration is higher than 18–20 µg/dL (500–550 nmol/L), thereby excluding the diagnosis of primary adrenal insufficiency

Treatment

- **Patient and family education:** Patients should understand the reason for life-long replacement therapy, the need to increase the dose of glucocorticoid during minor or major stress.
- **Glucocorticoid replacement therapy:** Should be treated with hydrocortisone, the natural glucocorticoid, daily dose is 10–15 mg/meter square body surface area (BSA) and can be administered in two to three divided doses with one half to two-thirds of the total daily dose being given in the morning.
- **Mineralocorticoid replacement therapy:** Fludrocortisone (9-alpha-fluorohydrocortisone) in a dose of 0.05–0.2 mg daily should be taken in the morning.
- **Liberal salt intake**

DIABETES INSIPIDUS

Diabetes insipidus (DI) is an endocrine disorder characterized by excretion of large volumes of hypotonic urine, the underlying cause being either a deficiency of

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the hormone arginine vasopressin (AVP) secreted from the posterior pituitary gland (central DI), or resistance to the actions of AVP in the kidneys (nephrogenic DI). Large volumes of urine excretion, also known as polyuria (typically over 4 L per day), is the hallmark of DI. The urine of DI has been classically described as insipid (tasteless), hypotonic and dilute.

CLINICAL FEATURES

- Passage of large volume of dilute urine (usually >4 liters/daily).
- Excessive thirst often resulting in disturbance of sleep.
- In several occasions, co-existing conditions can provide clues towards the possible etiology causing DI.
- Patients with hypophysitis can present with concomitant symptoms of anterior pituitary hormonal dysfunction including fatigue, erectile dysfunction, weight changes, loss of libido, galactorrhea, and amenorrhea.
- Headaches, visual field defects, or cranial nerve palsies can be observed along with DI in case of central nervous system (CNS) tumors, hypophysitis, or a pituitary adenoma.

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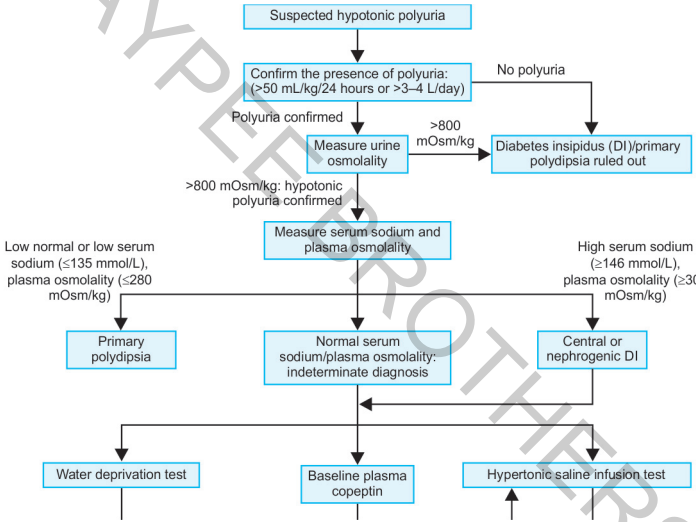
INVESTIGATIONS (FIG. 1)



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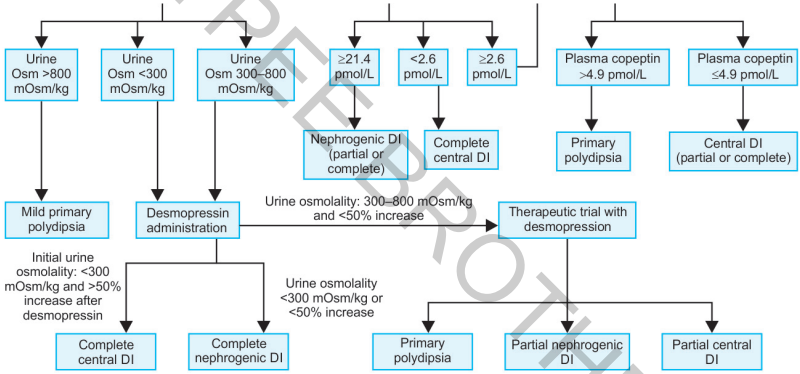

Fig. 1: Algorithm for diagnosis of the various types of polyuria polydipsia syndromes.

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OTHER INVESTIGATIONS

- **Measurement of plasma AVP:** Plasma AVP should be low or relatively low in central DI for the elevated plasma osmolality. In nephrogenic DI, as there is no deficiency of AVP.
- **Measurement of plasma copeptin**

TREATMENT

- **Liberal fluid replacement:** At a rate no greater than 500–750 mL/h. A good rule of thumb is to reduce serum sodium by 0.5 mmol/L (0.5 mEq/L) every hour. The water deficit may be calculated on the basis of the assumption that body water is approximately 60% of body weight.
- **Desmopressin:** In patients with central DI, desmopressin is the drug of choice. A synthetic analogue of antidiuretic hormone (ADH), desmopressin is available in subcutaneous, IV, intranasal, and oral preparations. Generally, it can be administered 2–3 times per day. Patients may require hospitalization to establish fluid needs. Frequent electrolyte monitoring is recommended during the initial phase of treatment.

  Monitor for fluid retention and hyponatremia during initial phase of therapy. Take record of intake-output chart and the frequency and volume of urination, and inquire about thirst. Monitor serum sodium, 24-hour urinary volumes, and specific gravity.
- Alternatives to desmopressin as pharmacologic therapy for DI include synthetic vasopressin and the nonhormonal agents chlorpropamide, carbamazepine, thiazides, and nonsteroidal anti-inflammatory drugs (NSAID's).

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DIABETES MELLITUS

It is a group of heterogeneous, complex metabolic disorder characterized by elevated blood glucose concentrations secondary to either resistance to the action of insulin or insufficient insulin secretion, or both. The most common classifications include Type 1 diabetes mellitus, Type 2 diabetes mellitus, and gestational diabetes.

CLINICAL FEATURES

- Usually, gradual in adults but acute in children
- Polyuria or excessive urination
- Polydipsia or intense thirst
- Nocturia
- Polyphagia or excessive feeding
- Unintentional weight loss
- Weakness and lassitude and fatigue
- Pruritus vulvae in females and balanitis or balanoposthitis in males.
- Leg cramps, crops of recurrent boils, loss of libido and erectile dysfunction in middle age
- Blurring of vision may develop
- Increased frothy urine or pedal swelling
- Tingling and numbness of hands and feet
- Frequent change of ophthalmic glasses

DIAGNOSIS

Diagnostic criteria by the American Diabetes Association (ADA) include the following:

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- A fasting plasma glucose (FPG) level of 126 mg/dL (7.0 mmol/L) or higher, *or*
- A 2-hour plasma glucose level of 200 mg/dL (11.1 mmol/L) or higher during a 75-g oral glucose tolerance test (OGTT), *or*
- A random plasma glucose of 200 mg/dL (11.1 mmol/L) or higher in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis *or*
- A hemoglobin A1c (HbA1c) level of 6.5% or higher

Treatment

- **Diet:**
  - Low calorie balanced diet (1200 to 2000 kcal/day depending on body weight).
  - Low carbohydrate, low fat, high protein diet with plenty of dark green leafy vegetables and yellow citrus fruits need to be consumed.
- **Physical exercise:** At least 45 to 60 minutes per day must be encouraged.
- **Pharmacotherapy:** Early initiation of pharmacologic therapy is associated with improved glycemic control and reduced long-term complications in type 2 diabetes.

Drug classes used for the treatment of type 2 diabetes include the following:

- **Biguanides:** Metformin
- **Sulfonylureas:** Glimepiride, gliclazide
- **Meglitinide derivatives:** Repaglinide
- **Alpha-glucosidase inhibitors (AGI):** Acarbose, voglibose
- **Thiazolidinediones (TZDs):** Pioglitazone

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- **Glucagon-like peptide-1 (GLP-1) agonists:** Liraglutide, dulaglutide, exenatide, semaglutide
- **Dipeptidyl peptidase IV (DPP-4) inhibitors:** Sitagliptin, vildagliptin, saxagliptin, linagliptin, teneligliptin, alogliptin
- **Selective sodium-glucose transporter-2 (SGLT-2) inhibitors:** Canagliflozin, dapagliflozin, empagliflozin, remogliflozin
- **Insulins:** Insulin is the drug of choice in type 1 diabetes mellitus. In type 2 diabetes mellitus, insulin is administered only if oral drugs fail and in special situations
- **Dopamine agonists:** Bromocriptine
- **Anti-inflammatory:** Hydroxychloroquine

DIABETIC KETOACIDOSIS

It is an acute life-threatening complication in people living with diabetes mellitus, predominantly in those with Type 1 diabetes mellitus. It results from the deficiency of insulin when the body switches to start using free fatty acids and produce acidic ketone bodies that cause most of the symptoms and complications.

CLINICAL FEATURES

Usually sudden in onset and it is an endocrine emergency. Patients usually present with various symptoms, such as excessive thirst, frequent urination, anorexia, nausea, vomiting, abdominal pain, weakness or fatigue, shortness of breath, fruity scented breath, confusion, Kussmaul

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breathing. Patients give history of failure to comply with insulin therapy or missed insulin injections due to vomiting or psychological reasons or history of mechanical failure of insulin infusion pump. Evidence of intercurrent infection as the precipitant of DKA, such as fever, cough, burning micturition, chills and rigor, dyspnea may also be present.

INVESTIGATIONS

- **Elevated blood sugar (consistently:** >300 mg/dL)
- **Plasma ketones:** Positive
- **Urinary ketones:** Positive
- **Arterial blood gas (ABG):** Reveals metabolic acidosis with low bicarbonate

Treatment

Managing diabetic ketoacidosis (DKA) in an intensive care unit during the initial 24–48 hours always is preferable. When treating patients with DKA, the following points must be considered and closely monitored:

- Correction of fluid loss by rapid rehydration with 4–6 liters of isotonic saline within 12 hours.
- Correction of hyperglycemia with Insulin 6–8 units per hour by IV infusion.
- Correction of acid-base balance with bicarbonate IV if plasma pH is below 7.2.
- Correction of electrolyte imbalance, particularly potassium with IV potassium, 1 ampoule to each bottle of saline infusion from 3rd bottle onwards under ECG (electrocardiograph) control.

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- Correction of intercurrent infection with Broad spectrum antibiotics.
- Insulin infusion is to be continued till ketosis clears up. Once blood sugar reaches around 250 mg%, saline is replaced by 5% dextrose saline.
- Patient may be started on multiple subcutaneous insulin injections once patient starts taking oral feeds.

HYPERKALEMIA

It refers to an elevated serum concentration of potassium (K^+) greater than approximately 5.0–5.5 mEq/L in adults.

CLINICAL FEATURES

Most individuals with hyperkalemia are asymptomatic. When present, symptoms are nonspecific and predominantly related to muscular or cardiac function. Weakness and fatigue are the most common complaints. Occasionally, patients may report frank muscle paralysis, dyspnea, palpitations, chest pain, nausea or vomiting, paresthesias.

On examination findings include the following:

- Vital signs usually normal, except occasionally in bradycardia due to heart block or tachypnea due to respiratory muscle weakness
- Muscle weakness and flaccid paralysis
- Depressed or absent deep tendon reflexes

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