Q: Enumerate the hormones secreted by anterior pituitary

Each of these hormones plays a crucial role in maintaining homeostasis and regulating various physiological processes. Their dysregulation can lead to a multitude of disorders, making the anterior pituitary a critical master component of the endocrine system.

- **Growth Hormone (GH)**:
    - Stimulates growth and cell reproduction in humans and other animals.
    - Regulates metabolic processes including protein synthesis and lipolysis.
- **Thyroid-Stimulating Hormone (TSH)**:
    - Stimulates the thyroid gland to produce thyroid hormones (T3 and T4).
    - Regulates metabolic rate, energy expenditure, and overall homeostasis.
- **Adrenocorticotropic Hormone (ACTH)**:
    - Stimulates the adrenal cortex to produce cortisol.
    - Regulates stress response, metabolism, and immune system.
- **Follicle-Stimulating Hormone (FSH)**:
    - In females, stimulates the growth of ovarian follicles and regulates the menstrual cycle.
    - In males, stimulates spermatogenesis.
- **Luteinizing Hormone (LH)**:
    - In females, triggers ovulation and stimulates the secretion of progesterone.
    - In males, stimulates the Leydig cells to produce testosterone.
- **Prolactin (PRL)**:
    - Stimulates milk production in females.
    - Regulates immune response and has over 300 functions in the body.
- **Melanocyte-Stimulating Hormone (MSH)**:
    - Stimulates the production and release of melanin by melanocytes in skin and hair.
- **Endorphins**:
    - Act as natural painkillers and mood elevators.
- **Enkephalins**:
    - Similar to endorphins, have analgesic effects.
- **Lipotropins**:
    - Stimulate the breakdown of fat stored in fat cells.
- **Beta-endorphins**:

    - Involved in pain modulation and behavioral effects.
- **Vasoactive Intestinal Peptides (VIP)**:
    - Have a range of effects, including vasodilation and regulation of smooth muscle activity.

Q: Factors Stimulating and inhibiting Secretion of Growth Hormone (GH)

Stimulators

- **Growth Hormone-Releasing Hormone (GHRH)**:
    - Produced by the hypothalamus, it directly stimulates the anterior pituitary to release GH.
- **Sleep**:
    - GH secretion is closely tied to the sleep cycle, particularly during deep, slow-wave sleep.
- **Physical Exercise**:
    - Aerobic and anaerobic activities stimulate GH release.
- **Amino Acids**:
    - Arginine and Lysine have been shown to stimulate GH release.
- **Low Blood Sugar (Hypoglycemia)**:
    - Triggers a counter-regulatory response that includes GH secretion.
- **Stress**:
    - Physical and emotional stress can lead to increased GH secretion.
- **Nutritional Status**:
    - Fasting or low levels of fatty acids can stimulate GH release.
- **Sex Hormones**:
    - Estrogen and Testosterone can modulate GH secretion.
- **Ghrelin**:
    - A hormone produced by the stomach, it has been found to stimulate GH release.
- **Alpha-Adrenergic Agonists**:
    - Drugs like clonidine can stimulate GH release.

Factors Inhibiting Secretion of Growth Hormone

- **Somatostatin (Growth Hormone-Inhibiting Hormone)**:
    - Produced by the hypothalamus, it inhibits GH release.
- **High Blood Sugar (Hyperglycemia)**:

    - Elevated glucose levels inhibit GH secretion.
- **Free Fatty Acids**:
    - Elevated levels can inhibit GH secretion.
- **Aging**:
    - GH secretion generally decreases with age.
- **Obesity**:
    - Excess adipose tissue is associated with reduced GH secretion.
- **Chronic Stress**:
    - While acute stress can stimulate GH release, chronic stress has an inhibitory effect.
- **Glucocorticoids**:
    - High levels of steroids like cortisol can inhibit GH.
- **Somatomedins (IGF-1 and IGF-2)**:
    - These GH-induced liver hormones can exert a negative feedback effect on GH secretion.
- **Beta-Adrenergic Agonists**:
    - Drugs like salbutamol can inhibit GH release.
- **Prolactin**:
    - High levels can inhibit GH secretion.

Category	Factors Stimulating GH Secretion	Factors Inhibiting GH Secretion
Genetic Factors	GH1 gene on chromosome 17 (q22-24)	-
Hormones	Growth Hormone-Releasing Hormone (GHRH), Ghrelin (also produced in large quantities by the stomach)	Somatostatin, Prolactin, Somatomedins (IGF-1, IGF-2)
Physiological States	Sleep, Physical Exercise, Physical Stress, Trauma, Acute Illness, Puberty, Fasting, Hypoglycemia	High Blood Sugar (Hyperglycemia), Aging, Obesity, Chronic Stress, Hypothyroidism
Nutritional Factors	Amino Acids (Arginine, Lysine), Fasting or low levels of fatty acids	Free Fatty Acids
Sex Hormones	Estrogen, Testosterone	-

Pharmacological Agents	Alpha-Adrenergic Agonists (e.g., clonidine)	Glucocorticoids, Beta-Adrenergic Agonists (e.g., salbutamol)

Q: Functions of Growth Hormone

Growth and Development

- **Linear Growth**: Stimulates growth plates in long bones
- **Cell Proliferation**: Increases the number of cells in tissues
- **Organ Growth**: Promotes the growth of internal organs

Protein Metabolism

- **Protein Synthesis**: Enhances amino acid uptake and protein synthesis in muscle and other tissues
- **Decreased Protein Oxidation**: Reduces protein catabolism

Carbohydrate Metabolism

- **Gluconeogenesis**: Stimulates the liver to produce glucose from amino acids
- **Insulin Resistance**: Induces a state of insulin resistance to ensure glucose availability for growing tissues

Lipid Metabolism

- **Lipolysis**: Stimulates the breakdown of triglycerides into free fatty acids
- **Decreased Lipogenesis**: Reduces the rate of fatty acid synthesis

Mineral Metabolism

- **Calcium Retention**: Increases intestinal calcium absorption
- **Phosphate Homeostasis**: Regulates serum phosphate levels

Endocrine Functions

- **Insulin-Like Growth Factor-1 (IGF-1) Production**: Stimulates the liver to produce IGF-1, which has growth-promoting effects
- **Thyroid Hormone Interaction**: Enhances the conversion of T4 to T3

Immune System

- **Immune Modulation**: Enhances the production of cytokines and stimulates the proliferation of T lymphocytes

Central Nervous System

- **Neuroprotection**: Provides protective effects on neurodegenerative processes
- **Cognitive Function**: Involved in learning and memory processes

Miscellaneous Functions

- **Cell Regeneration**: Promotes healing and tissue repair
- **Lactation**: Involved in the milk-production process in females
- **Water and Electrolyte Balance**: Affects renal function to some extent

Q: Indications for Growth Hormone Therapy in Children

Growth Hormone Deficiency (GHD)

- Confirmed deficiency through GH stimulation tests
- Short stature with slow growth velocity
- Congenital GHD due to genetic mutations or structural abnormalities

Idiopathic Short Stature (ISS)

- Height significantly below the mean for age and sex
- Absence of other identifiable causes of short stature

Turner Syndrome

- Confirmed diagnosis through karyotype analysis
- Short stature commonly associated with the syndrome

Prader-Willi Syndrome

- Genetic confirmation of the syndrome
- Short stature, hypotonia, and developmental delays

Chronic Renal Insufficiency

- Growth failure despite optimal medical management
- Pre-transplant patients to improve growth outcomes

Small for Gestational Age (SGA)

- Birth weight and/or length below -2 SD for gestational age
- Failure to catch-up growth by age 2-4 years

Noonan Syndrome

- Confirmed diagnosis through genetic testing
- Associated growth failure

SHOX Gene Haploinsufficiency

- Short stature homeobox-containing gene deficiency
- Short stature with or without skeletal abnormalities

Cachexia or Muscle Wasting Conditions

- Conditions like HIV-associated muscle wasting
- Severe burns or major surgeries leading to catabolic states

Cystic Fibrosis

- Growth failure despite optimal nutritional and medical management

Intrauterine Growth Retardation (IUGR)

- Persistent growth failure postnatally

Pubertal Delay

- Delayed puberty with associated growth failure

Contraindications

- Active malignancy
- Closed epiphyses
- Severe obesity
- Uncontrolled diabetes

Precautions

- Regular monitoring of glucose levels due to potential diabetogenic effect
- Monitoring of thyroid function, as GH can induce hypothyroidism
- Monitoring for signs of intracranial hypertension

Q: What are the causes of Dwarfism? How will you investigate such a case

Causes of Dwarfism in Children

Genetic Causes

- Achondroplasia: Most common form of short-limbed dwarfism
- Hypochondroplasia: Milder form of Achondroplasia
- Diastrophic Dysplasia: Autosomal recessive disorder affecting cartilage and bone development
- Spondyloepiphyseal Dysplasias: Affects vertebrae and long bones
- Osteogenesis Imperfecta: Brittle bone disease

Hormonal Causes

- Growth Hormone Deficiency: Lack of GH secretion
- Hypothyroidism: Congenital or acquired
- Cushing's Syndrome: Excess cortisol affecting growth

Nutritional Causes

- Malnutrition: Lack of essential nutrients affecting growth
- Rickets: Vitamin D deficiency

Metabolic Causes

- Glycogen Storage Diseases: Affecting liver and muscle function
- Mucopolysaccharidoses: Enzyme deficiencies leading to abnormal bone growth

Syndromic Causes

- Turner Syndrome: Affects females, missing or incomplete X chromosome
- Prader-Willi Syndrome: Genetic disorder causing poor muscle tone and feeding difficulties
- Noonan Syndrome: Autosomal dominant disorder affecting multiple systems

Other Causes

- Chronic Illness: Such as renal disease or gastrointestinal diseases
- Iatrogenic: Secondary to chemotherapy or radiation
- Unknown: Idiopathic short stature

Investigation Plan for a Case of Dwarfism

Initial Assessment

- Detailed history: Family history, prenatal and perinatal history, growth patterns
- Physical Examination: Anthropometric measurements, dysmorphic features

Laboratory Tests

- Complete Blood Count: To rule out anemia or infection
- Serum Electrolytes: To assess renal function
- Thyroid Function Tests: T3, T4, TSH
- IGF-1 and IGFBP-3: Indicators of GH action
- Serum Calcium and Phosphorus: To rule out rickets

Hormonal Assays

- GH Stimulation Test: To confirm GH deficiency
- Cortisol and ACTH levels: To rule out Cushing's syndrome

Genetic Testing

- Karyotyping: For suspected chromosomal disorders like Turner Syndrome
- Molecular Genetic Tests: For specific mutations in conditions like Achondroplasia

Imaging Studies

- X-rays: Skeletal survey to assess bone age and abnormalities
- MRI of the Brain: To evaluate pituitary and hypothalamic regions
- Ultrasound: Renal and hepatic assessment in cases of syndromic dwarfism

Specialized Tests

- Dual-Energy X-ray Absorptiometry (DEXA): Bone density
- Echocardiogram: In cases of suspected cardiac anomalies in syndromic dwarfism

Consultations

- Pediatric Endocrinologist: For hormonal imbalances
- Geneticist: For suspected genetic disorders
- Orthopedic Surgeon: For skeletal deformities

Q: Causes of hypotonic polyuria

- Polyuria is defined as excretion of a urinary volume >150 ml/Kg/24 hours at birth, >100-110 ml/Kg/24 hours up to the age of 2 years, and >50 ml/Kg/24 hours in older children or adults.
- A hypotonic urine is typically defined as a urine with an osmolality of <300 mOsm/Kg

CENTRAL (NEUROGENIC) DIABETES INSIPIDUS

- Congenital (congenital malformations, autosomal dominant, arginine vasopressin [AVP] neurophysin gene mutations)
- Drug or toxin induced (ethanol, diphenylhydantoin, snake venom)
- Granulomatous (histiocytosis, sarcoidosis)
- Neoplastic (craniopharyngioma, germinoma, lymphoma, leukemia, meningioma, pituitary tumor; metastases)
- Infectious (meningitis, tuberculosis, encephalitis)
- Inflammatory, autoimmune (lymphocytic infundibulo - neurohypophysitis)
- Trauma (neurosurgery, deceleration injury)
- Vascular (cerebral hemorrhage or infarction, brain death)
- Idiopathic

OSMORECEPTOR DYSFUNCTION

- Granulomatous (histiocytosis, sarcoidosis)
- Neoplastic (craniopharyngioma, pinealoma, meningioma, metastases)
- Vascular (anterior communicating artery aneurysm or ligation, intrahypothalamic hemorrhage)
- Other (hydrocephalus, ventricular or suprasellar cyst, trauma, degenerative diseases)
- Idiopathic

INCREASED AVP METABOLISM: Pregnancy

NEPHROGENIC DIABETES INSIPIDUS

- Congenital (X-linked recessive, AVP V2 receptor gene mutations, autosomal recessive or dominant, aquaporin-2 water channel gene mutations)
- Drug induced (demeclocycline, lithium, cisplatin, methoxyflurane)
- Hypercalcemia
- Hypokalemia
- Infiltrating lesions (sarcoidosis, amyloidosis)
- Vascular (sickle cell anemia)
- Mechanical (polycystic kidney disease, bilateral ureteral obstruction)
- Solute diuresis (glucose, mannitol, sodium, radiocontrast dyes)
- Idiopathic

PRIMARY POLYDIPSIA

- Psychogenic (schizophrenia, obsessive-compulsive behaviors)
- Dipsogenic (downward resetting of thirst threshold, idiopathic or similar lesions, as with central

Q: How will you assess a child presenting with features of Diabetes Insipidus

Assessment of a Child Presenting with Features of Diabetes Insipidus

Initial Clinical Evaluation

- **History Taking**: Assess for polyuria, polydipsia, nocturia, and dehydration symptoms.
- **Physical Examination**: Evaluate for signs of dehydration, weight loss, and neurological symptoms.

Laboratory Investigations

Basic Tests

- **Urine Osmolality**: Low osmolality (<300 mOsm/kg) suggests dilute urine.
- **Serum Osmolality**: Elevated levels (>295 mOsm/kg) indicate hyperosmolality.
- **Urine Specific Gravity**: Typically low (<1.005).
- **Blood Glucose**: To rule out diabetes mellitus.
- **Serum Electrolytes**: Assess sodium, potassium, and calcium levels for imbalances.

Confirmatory Tests

- **Water Deprivation Test**: Measures urine osmolality before and after water deprivation.
- **Vasopressin (ADH) Challenge Test**: Administration of synthetic ADH (Desmopressin) followed by measurement of urine osmolality.

Imaging Studies

- **MRI of the Brain**: To visualize the hypothalamus and pituitary gland for structural abnormalities.
- **Renal Ultrasound**: To rule out renal causes of polyuria.

Additional Tests

- **Serum ADH Levels**: Low in central DI and normal or high in nephrogenic DI.
- **Thyroid Function Tests**: To rule out hypothyroidism as a cause of polyuria.

Specialized Consultations

- **Endocrinology Consult**: For hormonal assays and management.
- **Nephrology Consult**: If renal causes are suspected.
- **Neurology Consult**: If DI is secondary to a neurological condition.

Treatment Plan

- **Desmopressin**: For central DI.
- **Thiazide Diuretics**: For nephrogenic DI.
- **Fluid Replacement**: To correct dehydration.
- **Diet Modification**: Low-sodium diet may be beneficial.

Monitoring and Follow-up

- **Regular Monitoring**: Of urine output, serum and urine osmolality, and electrolyte levels.
- **Growth and Development**: Regular assessments to ensure normal growth and development.

Genetic Counseling

- **Family History**: Assess for familial forms of DI.
- **Genetic Testing**: If familial DI is suspected.

Q: A 4-year-old child presents with polydipsia and polyuria. How will you establish a diagnosis of diabetes insipidus in this case? Discuss the diagnostic criteria and its management.

Diagnosis and Management of Diabetes Insipidus in a 4-Year-Old Child with Polydipsia and Polyuria

Diagnostic Criteria

Clinical Evaluation

- **Polyuria**: Urine output >2L/m^2/day or >50 mL/kg/day.
- **Polydipsia**: Excessive thirst and fluid intake >100 mL/kg/day.

Laboratory Investigations

Initial Tests

- **Urine Osmolality**: <300 mOsm/kg suggests dilute urine.
- **Serum Osmolality**: >295 mOsm/kg indicates hyperosmolality.
- **Urine Specific Gravity**: <1.005.

Confirmatory Tests