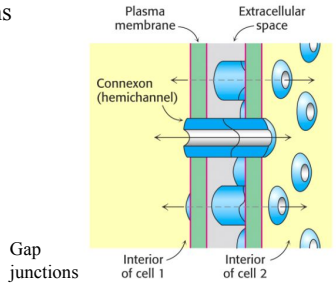
# Chapter 17
# Endocrine System

- Overview
- Hypothalamus and pituitary gland
- Other endocrine glands
- Hormones and their actions
- Stress and adaptation
- Eicosanoids and paracrine signaling
- Endocrine disorders

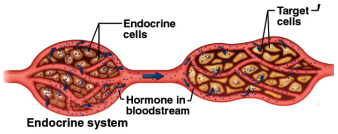
## Overview of Cell Communications

- Necessary for integration of cell activities
- Mechanisms

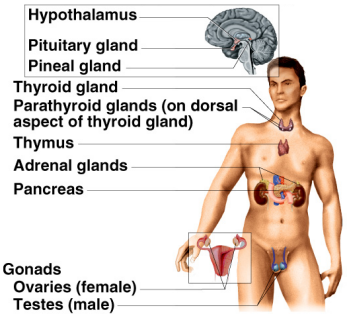



## Components of Endocrine System

- Hormone
- Target cells
- Endocrine system




## Endocrine Organs




- Major organs of endocrine system

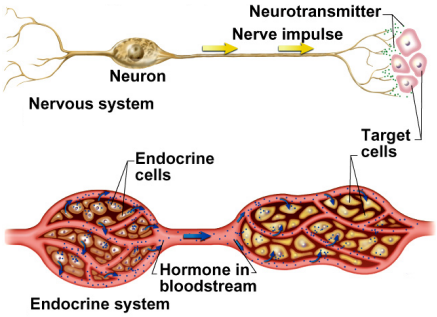
## Endocrine vs. Exocrine Glands

- Exocrine glands
- Endocrine glands
- Endocrine system

## Differences in Nervous and Endocrine Systems

- Means of communication
- Speed and persistence of response
- Adaptation to long-term stimuli
- Area of effect

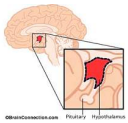
## Communication by the Nervous & Endocrine Systems

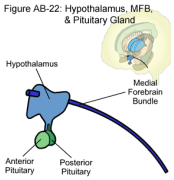



## Similarities in Nervous and Endocrine Systems

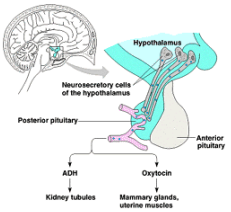
- Several chemicals function as both hormones and neurotransmitters
- Some hormones secreted by neuroendocrine cells (neurons)
- Both systems with overlapping effects on same target cells
- Systems regulate each other

## Hypothalamus

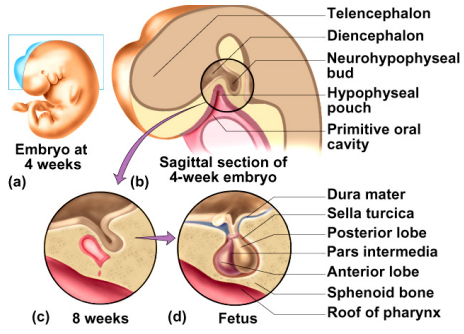




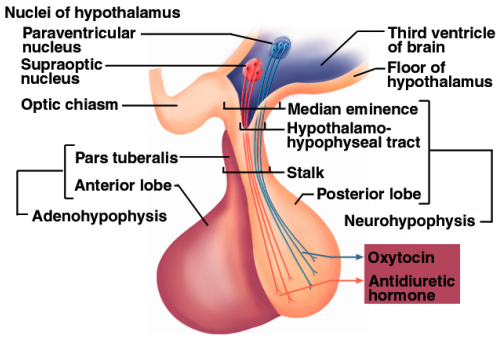

## Pituitary Gland (Hypophysis)



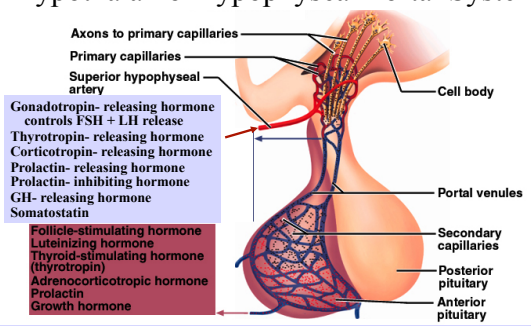

## Embryonic Development of Pituitary




## Pituitary Gland Anatomy and Hormones of the Neurohypophysis

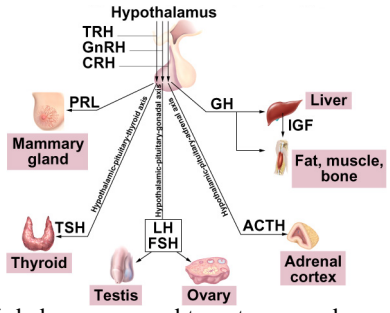


## Hypothalamo-Hypophyseal Portal System




- Hormones secreted by hypothalamus, travel in portal system to anterior pituitary
- Hormones (red box)secreted by anterior pituitary (under control of hypothalamic releasers and inhibitors)

## Anterior Pituitary Hormones

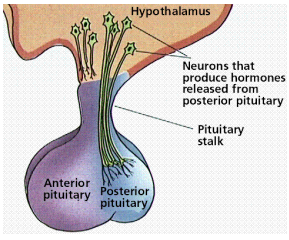



- Principle hormones and target organs shown
- Axis - refers to way endocrine glands interact

## Pituitary Hormones - Pars Intermedia

- Absent from adult human although present in fetus
- Reminant cells
  - produce POMC (pro-opiomelanocortin) which is processed into ACTH and endorphins
- Produces MSH in animals influencing pigmentation of skin, hair or feathers
  - not apparently present/functioning in humans

## Pituitary Hormones - Posterior Lobe




## Pituitary Hormone Actions:

Anterior Lobe Hormones

- FSH (secreted by gonadotrope cells)
- LH (secreted by gonadotrope cells)
- TSH (secreted by thyrotropes)

## Pituitary Hormone Actions:
Anterior Lobe Hormones

- ACTH or corticotropin (secreted by corticotropes)
- PRL (secreted by lactotropes)
- GH or somatotropin – see next 2 slides

## Growth Hormone

- Secreted by somatotropes of anterior pituitary
- Promotes tissue growth
- Functions of GH-IGF

## Growth Hormone and Aging

- Childhood and adolescence
- Adulthood
- Levels of GH

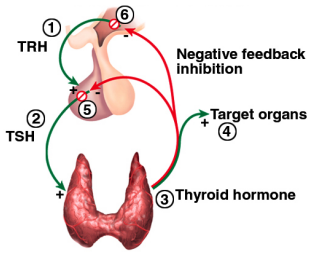
## Pituitary Hormone Actions:
Posterior Lobe Hormones

- ADH
  - targets kidneys to ↑ water retention, reduce urine
  - also functions as neurotransmitter
- Oxytocin
  - labor contractions, lactation
  - possible role sperm transport, emotional bonding

## Control of Pituitary:
Hypothalamic and Cerebral Control

- Anterior lobe control - releasing hormones and inhibiting hormones of hypothalamus
- Posterior lobe control - neuroendocrine reflexes

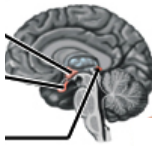
## Control of Pituitary:
Feedback from Target Organs




- Negative feedback
- Positive feedback

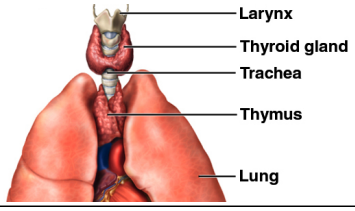
## Pineal Gland

- Peak secretion 1-5 yr. olds, by puberty 75% lower
- Produces serotonin by day, converts it to melatonin at night
- May regulate timing of puberty in humans
- Melatonin ↑ in SAD + PMS, ↓ by phototherapy
  - depression, sleepiness, irritability and carbohydrate craving

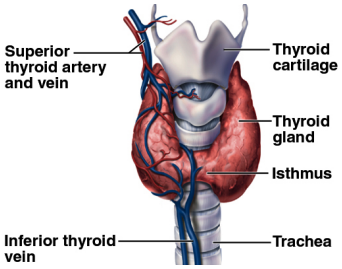



## Thymus

- Location: mediastinum, superior to heart
- Involution after puberty
- Secretes hormones that regulate development and later activation of T-lymphocytes
  - thymopoietin and thymosins

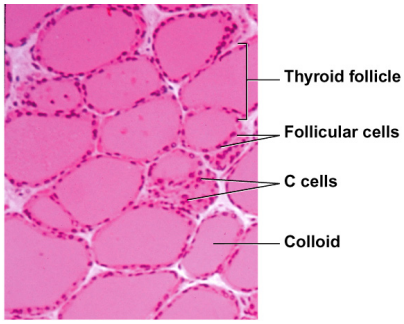



## Thyroid Gland Anatomy



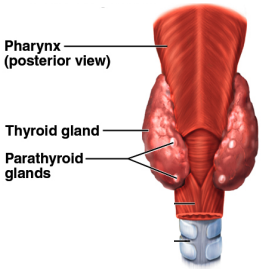

- Largest endocrine gland with high rate of blood flow
- Anterior and lateral sides of trachea
- 2 large lobes connected by isthmus

## Histology of the Thyroid Gland

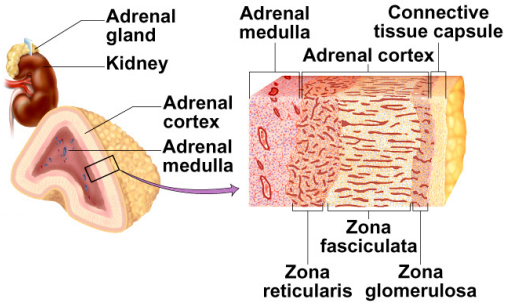



## Parathyroid Glands

- PTH release
  - ↑ blood $Ca^{+2}$ levels
  - promotes synthesis of calcitriol
    - ↑ absorption of $Ca^{+2}$
    - ↓ urinary excretion
    - ↑ bone resorption




## Adrenal Gland



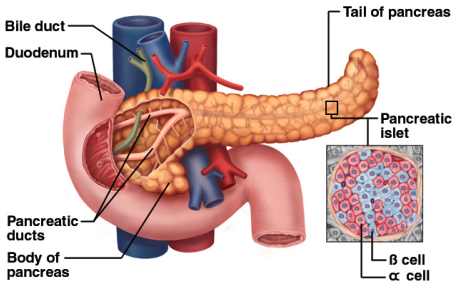
## Adrenal Medulla

- Sympathetic ganglion innervated by sympathetic preganglionic fibers
- Hormonal effect is longer lasting
- Stress causes medullary cells to stimulate cortex

## Adrenal Cortex

- Layers -- (outer) zona glomerulosa, (middle) zona fasciculata, (inner) zona reticularis
- Corticosteroids

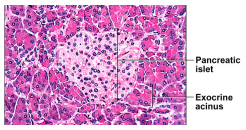
## Pancreas




- Retroperitoneal, inferior and dorsal to stomach

## Pancreatic Hormones

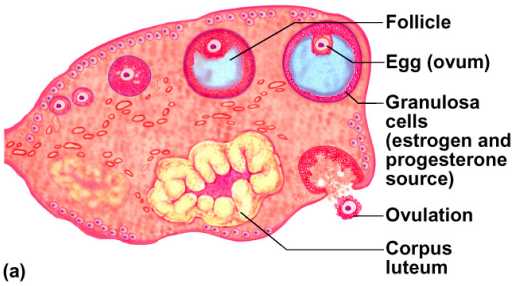
- 1-2 Million pancreatic islets producing hormones
  - 98% of organ produces digestive enzymes (exocrine)
- Insulin (from β cells)




## Pancreatic Hormones 2

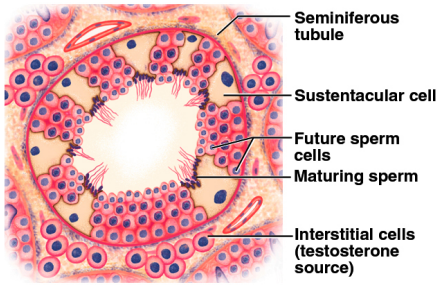
- Glucagon (from α cells)
- Somatostatin from delta (δ) cells)
- Hyperglycemic hormones raise blood glucose
- Hypoglycemic hormones lower blood glucose

## Histology of Ovary




Follicles = egg surrounded by granulosa cells

## Histology of Testis




Seminiferous tubules produce sperm.

## Endocrine Functions of Other Organs

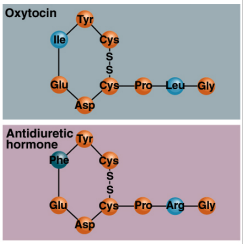
- Heart –
  - atrial natriuretic peptide released with an increase in BP
  - ↓ blood volume + ↓ BP by ↑ $Na^+$ and $H_2O$ loss by kidneys
- Skin
  - keratinocytes help produce D3, first step in synthesis of calcitriol
- Liver
  - converts vitamin D3 to calcidiol
  - source of IGF-I that works with GH
  - secretes about 15% of erythropoietin
  - secretes angiotensinogen (a prohormone)
    - precursor of angiotensin II, a vasoconstrictor

## Endocrine Functions of Other Organs

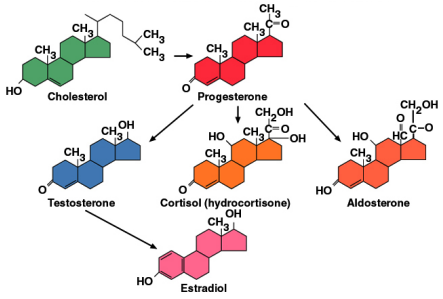
- Kidneys
  - converts calcidiol to calcitriol (active form of vitamin D)
    - ↑ absorption by intestine and inhibits loss in the urine
    - more $Ca^{+2}$ available for bone deposition
  - produces 85% of erythropoietin –
    - stimulates bone marrow to produce RBC's
  - convert angiotensinogen to angiotensin I
- Stomach and small intestines (10 enteric hormones)
  - coordinate digestive motility and secretion
- Placenta
  - secretes estrogen, progesterone and others
    - regulate pregnancy, stimulate development of fetus and mammary glands

## Hormone Chemistry

- Steroids
  - derived from cholesterol
    - sex steroids, corticosteroids
- Peptides and glycoproteins
  - OT, ADH; all releasing and inhibiting hormones of hypothalamus; most of anterior pituitary hormones
- Monoamines (biogenic amines)
  - derived from amino acids
    - catecholamines (norepinephrine, epinephrine, dopamine) and thyroid hormones

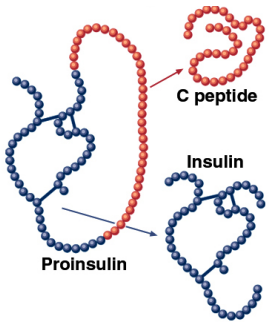



## Hormone Synthesis: Steroid Hormones



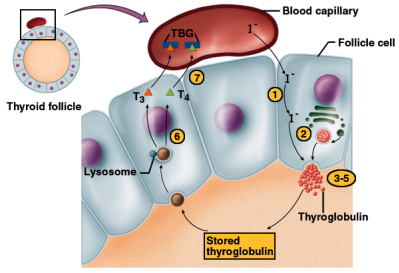

## Hormone Synthesis: Peptides

- Cellular steps
- Insulin formation



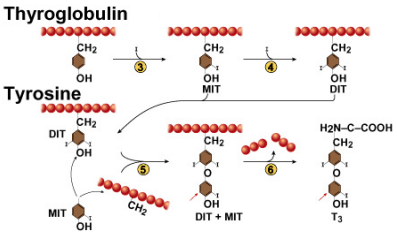
## Hormone Synthesis: Monoamines

## Thyroid Hormone Synthesis




**(1) $I^-$ transported into cell then (2) $I^-$ + thyroglobulin released into lumen (3-5 next slide) (6)TSH stimulates pinocytosis, lysosome liberates TH, carried by thyroxine-binding globulin**

## Thyroid Hormone Synthesis

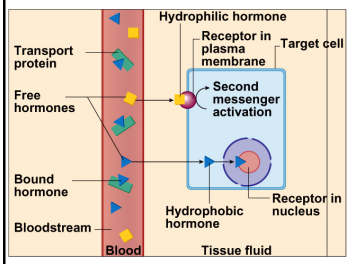



## Hormone Transport

- Monoamines and peptides are hydrophilic so mix easily with blood plasma
- Steroids and thyroid hormone are hydrophobic and must bind to transport proteins for transport
- Transport proteins in blood plasma

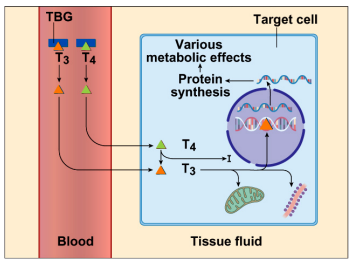
## Hormone Receptors

## Hormone Mode of Action



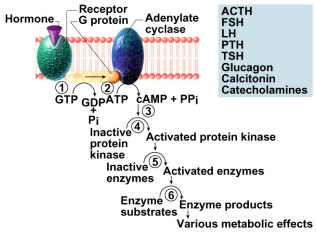

- Hydrophobic hormones (steroids and thyroid hormone) penetrate plasma membrane – enter nucleus
- Hydrophilic hormones (monoamines and peptides) can not pass through membrane so must bind to cell-surface receptors

## Thyroid Hormone Effects




## Hydrophilic Hormones: Mode of Action

### cAMP as Second Messenger

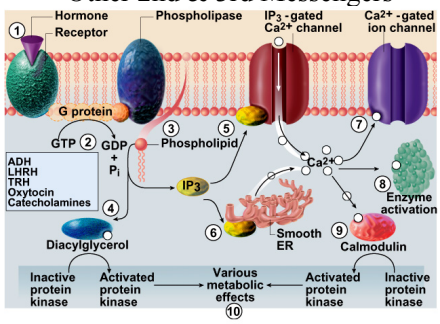



1) Hormone binding activates G protein
2) Activates adenylate cyclase
3) Produces cAMP
4) Activates kinases
5) Activates enzymes
6) Metabolic reactions: synthesis, secretion, change membrane potentials

Peptides and catecholamines bind to receptors in cell membrane

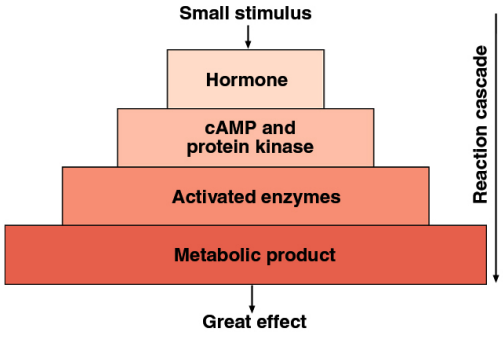
## Hydrophilic Hormones: Mode of Action

### Other 2nd & 3rd Messengers



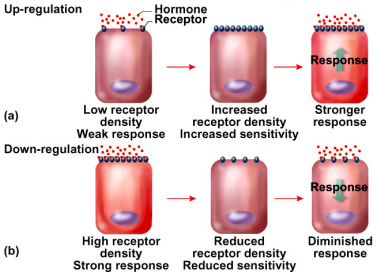

Hormones may use different second messengers in different tissues.

## Enzyme Amplification




## Hormone Clearance

## Modulation of Target Cell Sensitivity



## Hormone Interactions

## Stress and Adaptation

## Alarm Reaction

## Stage of Resistance

## Stage of Exhaustion

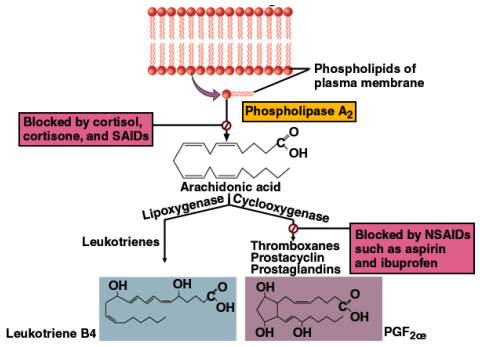
## Paracrine Secretions

- Chemical messengers that diffuse short distances and stimulate nearby cells
  - unlike neurotransmitters not produced in neurons
  - unlike hormones not transported in blood
- Examples and their functions
  - histamine from mast cells in connective tissue causes relaxation of blood vessel smooth muscle
  - nitric oxide from endothelium of blood vessels causes vasodilation
  - somatostatin from gamma cells inhibits secretion of alpha and beta cells in pancreas
  - catecholamines diffuse from adrenal medulla to cortex

## Eicosanoids: a Paracrine Secretion

- Derived from arachidonic acid (fatty acid)
- Hormone releases arachidonic acid from plasma membrane and 2 enzymes convert it into eicosanoids

## Eicosanoid Synthesis




## Endocrine Disorders

- Variations in hormone concentration and target cell sensitivity have noticeable effects on the body
- Hyposecretion – inadequate hormone release
  - tumor or lesion destroys gland
- Hypersecretion – excessive hormone release
  - tumors or autoimmune disorder

## Pituitary Disorders

- Hypersecretion of growth hormones
  - acromegaly
  - thickening of the bones and soft tissues
  - problems in childhood or adolescence
    - gigantism if oversecretion
    - dwarfism if hyposecretion


## Thyroid Gland Disorders

- Congenital hypothyroidism (↓ TH)
  - infant suffers abnormal bone development, thickened facial features, low temperature, lethargy, brain damage
- Myxedema (adult hypothyroidism, **↓ TH**)
  - low metabolic rate, sluggishness, sleepiness, weight gain, constipation, dry skin and hair, cold sensitivity, ↑ blood pressure and tissue swelling
- Endemic goiter (goiter = enlarged thyroid gland)
  - dietary iodine deficiency, no TH, no - feedback, ↑ TSH
- Toxic goiter (Graves disease)
  - antibodies mimic TSH, **↑TH**, exophthalmos

## Endemic Goiter

## Parathyroid Disorders

- Hypoparathyroid
  - surgical excision during thyroid surgery
  - fatal tetany 3-4 days
- Hyperparathyroid = excess PTH secretion
  - tumor in gland
  - causes soft, fragile and deformed bones
  - ↑ blood $Ca^{+2}$
  - renal calculi

## Adrenal Disorders

- Cushing syndrome is excess cortical secretion
  - causes hyperglycemia, hypertension, weakness, edema
  - muscle and bone loss occurs with protein catabolism
  - buffalo hump & moon face = fat deposition between shoulders or in face
- Adrenogenital syndrome (AGS)
  - adrenal androgen hypersecretion accompanies Cushing
  - causes enlargement of external sexual organs in children & early onset of puberty
  - masculinizing effects on women (deeper voice & beard growth)

## Diabetes Mellitus

- Signs and symptoms of hyposecretion of insulin
  - polyuria, polydipsia, polyphagia
  - hyperglycemia, glycosuria, ketonuria
    - osmotic diuresis : blood glucose levels rise above transport maximum of kidney tubules, glucose remains in urine, osmolarity ↑ and draws water into urine
- Transport maximum of glucose reabsorption
  - kidney tubules can not reabsorb glucose fast enough if no insulin is present
  - osmotic diuresis results due to excess glucose and ketones in tubules

## Types of Diabetes Mellitus

- Type I (IDDM) - 10% of cases
  - some cases have autoimmune destruction of β cells, diagnosed about age 12
  - treated with diet, exercise, monitoring of blood glucose and periodic injections of insulin or insulin pump
- Type II (NIDDM) - 90%
  - insulin resistance
    - failure of target cells to respond to insulin
  - 3 major risk factors are heredity, age (40+) and obesity
  - treated with weight loss program of diet and exercise,
  - oral medications improve insulin secretion or target cell sensitivity

## Pathology of Diabetes

- Acute pathology: cells cannot absorb glucose, rely on fat and proteins (weight loss + weakness)
  - fat catabolism ↑ FFA's in blood and ketone bodies
  - ketonuria promotes osmotic diuresis, loss of $Na^{+}$ + $K^{+}$
  - ketoacidosis occurs as ketones ↓ blood pH
    - if continued causes dyspnea and eventually diabetic coma
- Chronic pathology
  - chronic hyperglycemia leads to neuropathy and cardiovascular damage from atherosclerosis
    - retina and kidneys (common in type I), atherosclerosis leading to heart failure (common in type II), and gangrene

## Hyperinsulinism

- From excess insulin injection or pancreatic islet tumor
- Causes hypoglycemia, weakness and hunger
  - triggers secretion of epinephrine, GH and glucagon
    - side effects: anxiety, sweating and ↑ HR
- Insulin shock
  - uncorrected hyperinsulinism with disorientation, convulsions or unconsciousness