Hypothalamic Hormones

HI,
first of all, doctor didn't say anything that much on slides, but I tried to conclude everything could be important
it is an easy lecture, have fun #

- Hypothalamus → ADH & Oxytocin → neuro-secretory axons→ Posterior pituitary
- Hypothalamus → Hormones → network of capillaries (portal system)→ Anterior pituitary
- ACTH, TSH, LH, FSH (stimulatory control)
- GH, PRL, MSH (stimulatory and inhibitory control)

neurohormone

inhibited by dopamine.

Make skin darker

protects skin from UV

- **General characteristics of hypothalamic hormones:**

TRH, CRH, GHRH, GHIH, GnRH, Dopamine (DA)

- Small peptides and polypeptides (exception DA) of low M.W
- Needed in very low concentrations (*p*g)
- Have short $t_{1/2}$
- Act on receptors on plasma membrane

amino acid derivative

- **TRH=Thyroid Releasing Hormone (Protirelin)**

3 =Tri-peptide, synthetic analogs are available

Effective orally and I.V

Stimulates TSH synthesis and release

MOA: Activation of phospholipase C to increase intracellular IP3 & DAG

Also, TRH has been found to increase PRL release through 2nd messenger Ca^{++}

Mainly used:

- As a diagnostic tool (TRH test)
- To treat certain cases of hypothyroidism

Dose: 50 µg I.V, 5 mg orally, maximum response in 15-30 min, DOA 2-4 hrs

- **CRH=Coricotropin Releasing Hormone**

41 a.a peptide stimulates synthesis and release of ACTH, stress ↑ CRH release

Diagnostic use (CRH test)

- **GHRH (Hexarelin, Sermorelin)**

40 a.a peptide, synthetic preparations are available

Diagnostic use and in the management of certain cases of dwarfism (it is given SC)

- **GHIH (Somatostatin)**

14 a.a peptide

↓ secretion of GH, ACTH, TSH, Insulin, Glucagon, Gastrin, Serotonin

Its effects on blood glucose levels are dose dependent

Low doses → hypoglycemia (↓ glucagon secretion)

High dose → hyperglycemia (↓ insulin secretion)

Octreotide (given S.C) & **Lanreotide** (given I.M)

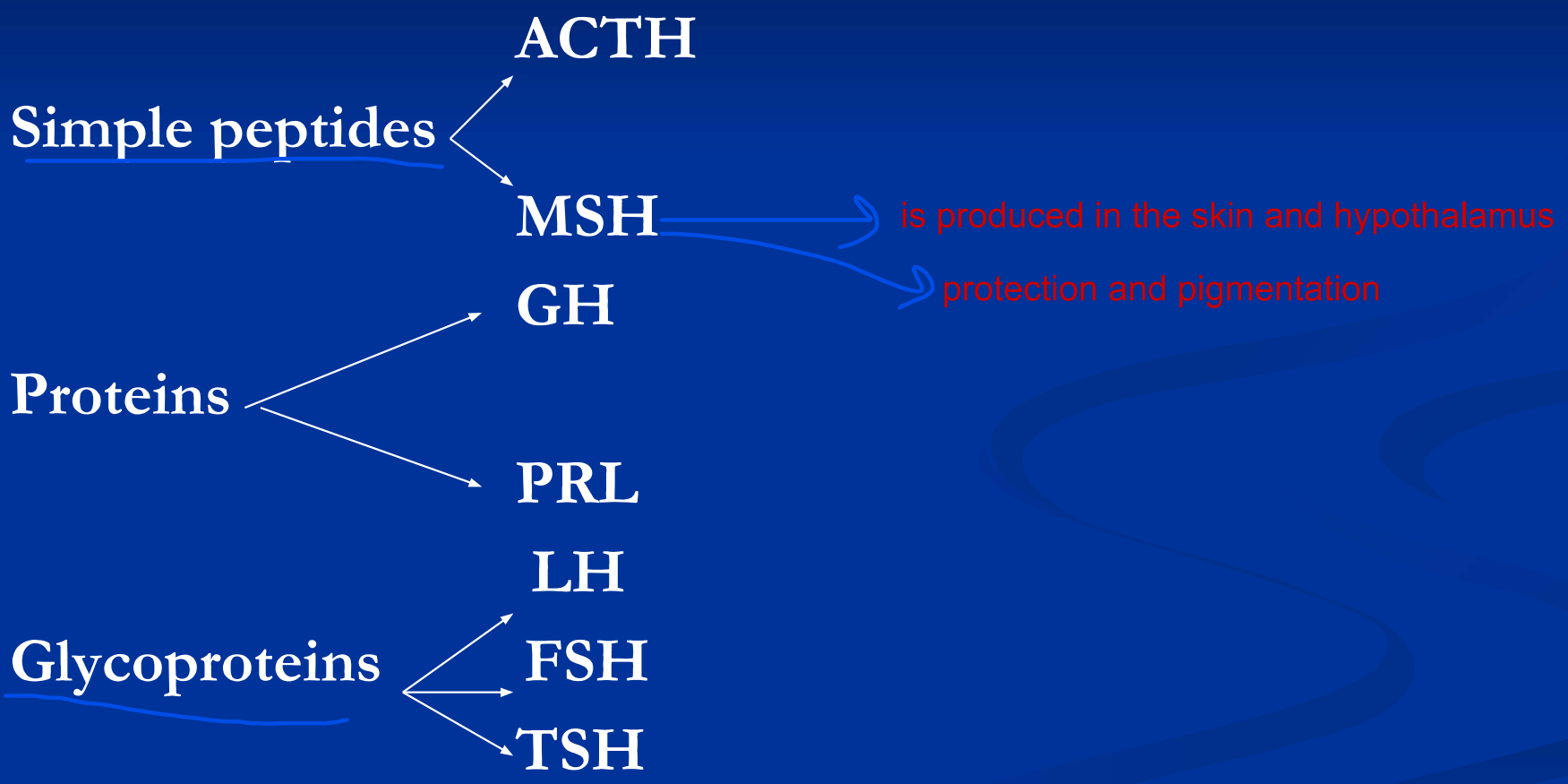
Synthetic analogs to somatostatin with longer $t_{1/2}$ are mainly used in the management of:

- Acromegaly
- Carcinoid syndrome → tumor affecting interchromatin cells in intestine leading to severe diarrhea, (so much release of serotonin)
- Insulinomas, gastrinomas → increase gastrin secretion.
  ↓ increase insulin even after your blood sugar drops too low.
- Esophageal varices → extremely dilated veins in the lower third of the esophagus. They are most often a consequence of portal hypertension
- ?? Diabetes mellitus

Major side effects: Gall bladder stone formation and platelet abnormalities

Pituitary Hormones

- **Anterior Pituitary Hormones**



- **Posterior Pituitary Hormones**

Simple peptides (9 a.a)

ADH (Vasopressin)

Oxytocin

- Hypothalamic hormones regulating the anterior pituitary hormones reach the anterior pituitary through a network of capillaries (portal system) whereas ADH and oxytocin reach the posterior pituitary via neurosecretory axons

Anterior Pituitary Hormones

Hypothalamic lesion or removal → ↓ Ant. Pit H's except PRL

Hypothalamic stimulation → ↑ Ant. Pit H's except PRL → mainly inhibition from hypothalamus dopamine

- TSH

↑ T_3 & T_4 through ↑ cAMP, ↑ Iodine uptake

↑ iodination and hydrolysis of thyroglobulin

** diagnostic use

- **ACTH**

Derived from larger precursor (Pro-opiocortin)

↑ cortisol release

Undergoes circadian rhythm

Acthar and Cosyntropin (tetracosactrin; Cortrosyn) are synthetic analogs

Uses:

- Diagnostic use (given I.V or I.M)
- Certain cases of adrenal insufficiency

synthesized insulin is animal insulin (beef or pig), pig insulin differs from human insulin in 1amino acid (less allergy) , not used on human (just for resarch)

- **Growth hormone (Somatropin)**

- Species specific
- MOA unclear, its effects believed to be mediated through IGFs (Somatomedins) which are formed in the liver , kidneys, muscles and other tissues
- GH stimulates growth of soft tissues and bones
- ↑ lipolysis
- ↑ gluconeogenesis & ↓ glucose utilization (diabetogenic effect)
- PRL-like activity

- **Factors ↑ GH release:**

follow the patient after administration , if there is a change in GH release (increase) , there is no problem

- Sleep, Arginin, Insulin, Hypoglycemia
- β-adrenergic antagonists, Clonidine, Bromocriptine and Levodopa in normal individuals

- **Factors ↓ GH release:**

- Bromocriptine in acromegalics
- Somatostatin synthetic analogs

lowers GH secretion when there is over secretion (acromegaly) and increase GH secretion in normal individuals . (not well understood)

- **Disorders affecting GH secreting cells:**

Hypersecretion → Gigantism, Acromegaly

children adults

R_x

- **Surgery** intranasal = to remove tumors
good outcomes = completely cure
- **Somatostatin synthetic analogs**
- **DA agonists (Bromocriptine; Cabergoline) and**
- **Pegvisomant (GH-receptor antagonist, given SC, major side effects include abnormal liver enzymes and some reports indicated increased growth of GH-secreting pituitary tumors)**

Hyposecretion of GH

- In children it leads to dwarfism manifested by a very short trunk, short neck, shortened arms and legs, average-size hands and feet, broad rounded chest…
- In adults Not so common but it may lead to a higher level of body fat, especially around the waist, anxiety and depression, decreased sexual function and interest, fatigue, less muscle…

Rx of dwarfism → GH replacement therapy

Rx of GH deficiency in adults → loss of weight, good sleep, high protein low carbohydrate diet, exercises ± GH replacement therapy

good lifestyle

GH replacement therapy

- GH-replacement therapy with S.C or I.M recombinant human GH preparations:
  - Somatropin (Humatrope)
  - Somatrem (Protropin)
- Mecasermin (recombinant human IGF-1); mecasermin rinfabate (recombinant human IGF-1 +IGF binding protein-3=IGFBP-3), given SC in dwarf with IGF-1 deficiency not responding to GH, hypoglycemia is a major side effect

given subcutaneously every day till puberty. (preferable at night)
given intramuscular twice or 3 times A week more convenient .

Mecasermin rinfabate is similar to Mecasermin in that both drugs contain recombinant DNA origin insulin-like growth factor 1 (IGF-1). Mecasermin rinfabate however, is already bound to recombinant DNA origin insulin-like growth factor binding protein 3 (IGFBP-3). The binding of IGF-1 to IGFBP-3 is said to extend the half life and reduce the clearance of IGF-1 in patients with growth hormone resistant syndromes and low levels of IGFBP-3 though this may represent <500 patients worldwide

Both mecasermin and mecasermin rinfabate are usually given SC

major side effect is psycho...

- Side effects of synthetic rHGH products:

Water retention, the development of antibodies to HGH, insulin resistance and diabetes, hypertension, carpal tunnel syndrome, abnormal bone growth, reduced life span, disturbed insulin metabolism, leukemia, overgrowth of connective tissue, and tumors, ↑ intracranial pressure with papilledema

oxytocin in male: increase sexual desire & help in ejaculation.

- **Prolactin (PRL)**

Ant. Pit; Placenta

** Dopamine (DA)

** Has GH-like activity

In ♂s PRL increases testosterone production by testes and hence spermatogenesis but ↑ PRL → ↓ LH & FSH → ♂ impotency & infertility

14 days of treatment

decrease sexual function

In ♀s:

- Breast development (puberty; pregnancy)
- Lactation
- ↑ PRL → ↓ LH & FSH (galactorrhea amenorrhea syndrome)

- **Factors/drugs ↑ PRL:**

- Pregnancy, sleep, nursing, stress (surgery, exercise)
- TRH, Estradiol, DA antagonists (antipsychotics= phenothiazines and haloperidol; metoclopramide..)
- Methyldopa, reserpine, diazepam, opiates, meclizine, imipramine…

- **Factors/drugs ↓ PRL:**

DA agonists (Bromocriptine, pergolide, levodopa)

apomorphine, clonidine , MAO inhibitors (pargyline)

drug of choice like when a breastfeeding mother lose her baby

- **Clinical uses to dopamine agonists:**

Bromocriptine, Cabergolin…

- Hyperprolactinemia in ♂s and ♀s irrespective of its causes (drug of choice)
- Suppression of lactation
- Acromegaly
- Parkinson's disease deficiency of dopamine release in nervus system
- Cushing's syndrome (Dopamine agonists have been found to inhibit ACTH release)
- DM type II

Dopamine agonists are given orally

Side effects:

Rare, pulmonary fibrosis; confusion; hallucinations; MI…