Poltava State Medical University

Lecture

HORMONAL DRUGS
ANTIDIABETIC DRUGS

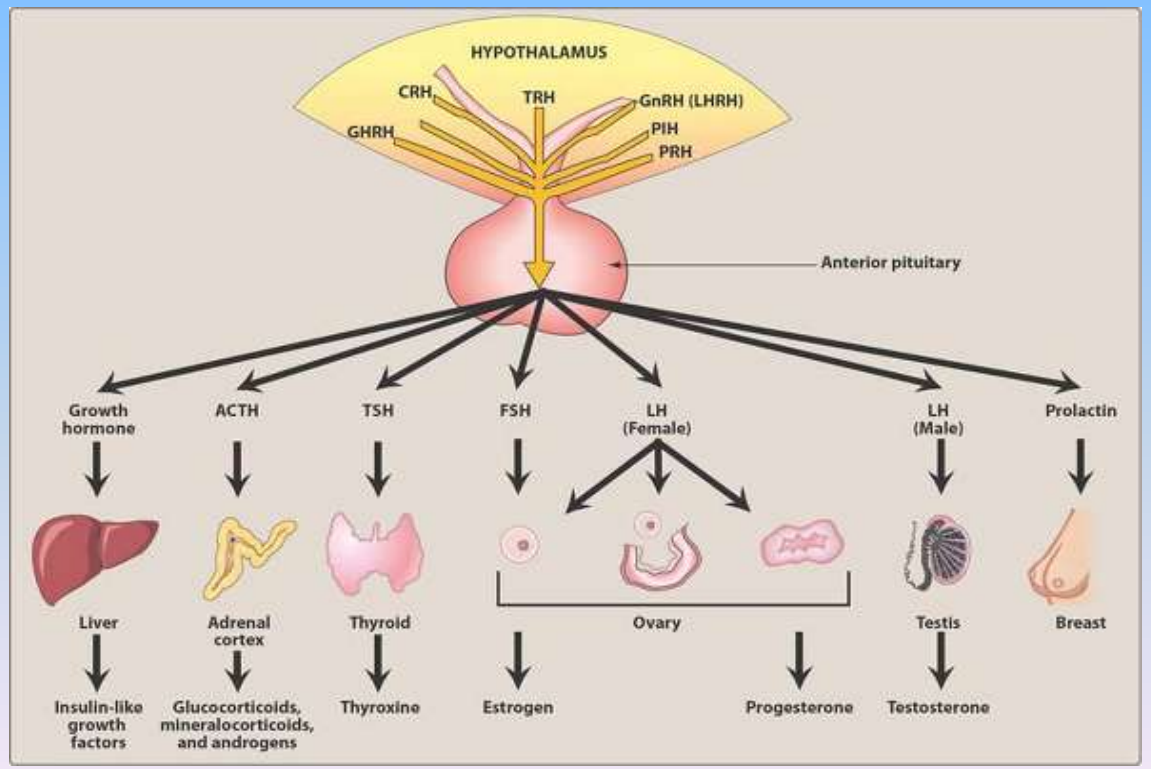
CONTENTS

1. Classification. Common concepts relating to hormonal preparations and hormonal therapy
2. Hypothalamic and pituitary hormones
3. Thyroid hormones and their antagonists
4. Hormones regulating Ca-P metabolism
5. Antidiabetic drugs. Insulin. Oral hypoglycemic drugs
6. Glucocorticoids and mineralcorticoids
7. Male gonadal hormones and related substances
8. Female gonadal hormones and related substances
9. Control tasks

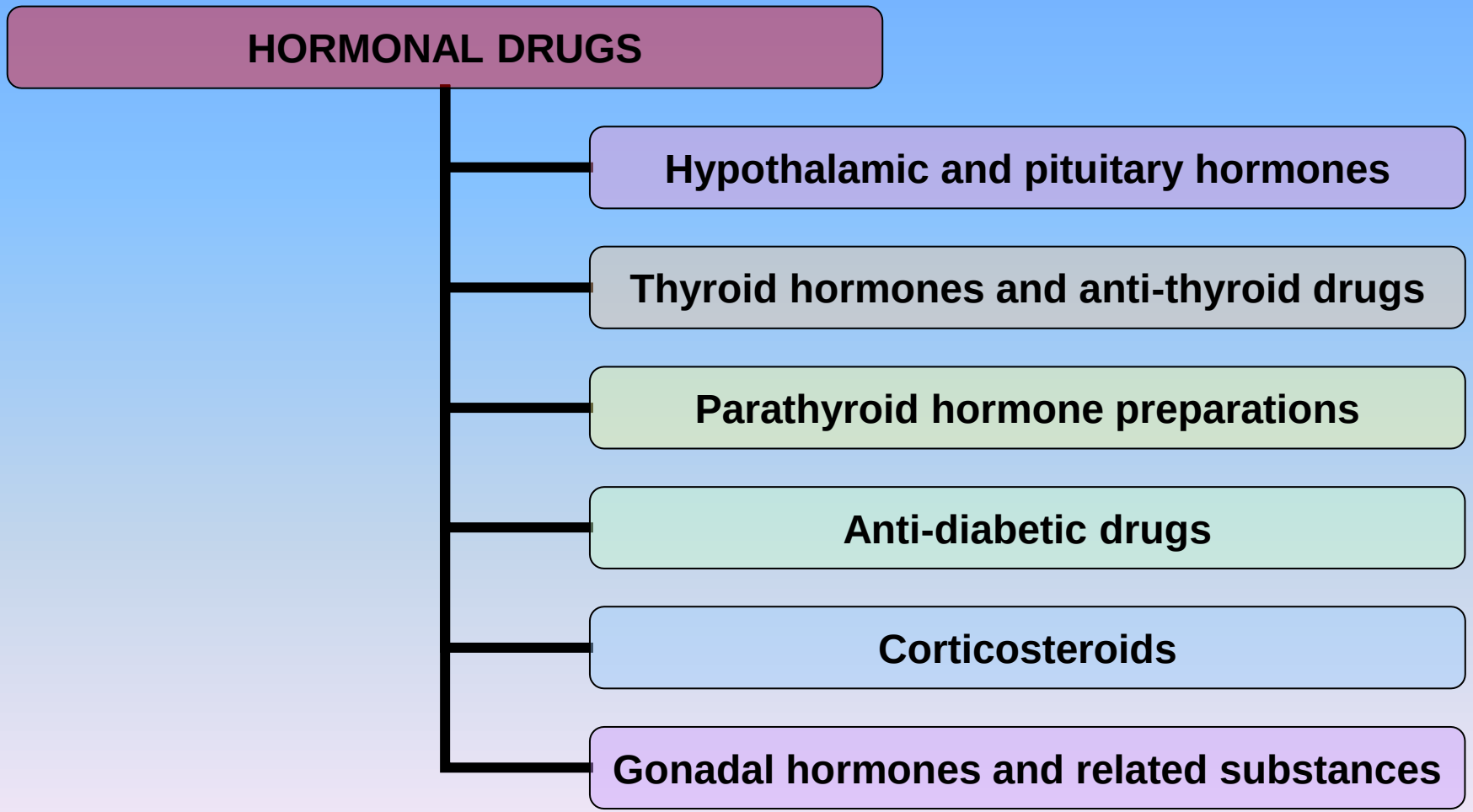
HORMONES AND HORMONAL PREPARATIONS

Hormones are substances produced by endocrine glands, which achieve humoral regulation of the functions of the organism.

Hormonal preparations are medicinal forms of hormones used for treatment of diseases.



MAIN GROUPS OF HORMONAL PREPARATIONS



CLASSIFICATION OF HORMONAL DRUGS

Classification of hormones on mode of action

A. *Kinetic hormones* (oxytocin, vasopressin)

B. *Morphogenous hormones* (somatotropin, thyroid hormones)

C. *Metabolic hormones*

1. Anabolic (androgens, insulin)
2. Catabolic (epinephrine, glucocorticoids).

Classification of hormones on chemical structure

A. *Amino acids derivatives* – epinephrine, L-thyroxine, Triiodthyronine hydrochloride

B. *Peptides* – Corticotropin, Somatotropin, Menopaustic gonadotropin, Chorionic gonadotropin, Oxytocin, Adiurecrin, Calcitonin, Parathyroidin, Insulin

C. *Steroids*

1. Glucocorticoides – Hydrocortisone acetate, Prednisolone, Dexamethasone, Triamcinolone, Flumetasone pivalate
2. Mineralcorticoides – Desoxycorticosterone acetate (DOCSA)
3. Estrogens – Estron, Estradiol benzoate, Ethinylestradiol
4. Progestins – Progesterone
5. Androgens – Testosterone propionate
6. Anabolic steroids – Retabolil, Phenobolinum, Methandrostenolonum.

HORMONES MECHANISMS OF ACTION

Hormones exert their effects through different mechanisms:

- by binding to the cell surface receptors (oxytocin, vasopressin, corticotropin, insulin etc.)
- by binding to intracellular cytoplasmic receptors (glucocorticoids, mineralcorticoids, estrogens, progestins)
- by interaction with nuclear receptors (thyroxine, triiodthyronine)

HORMONAL THERAPY

Hormonal therapy is the therapy by hormonal preparations.

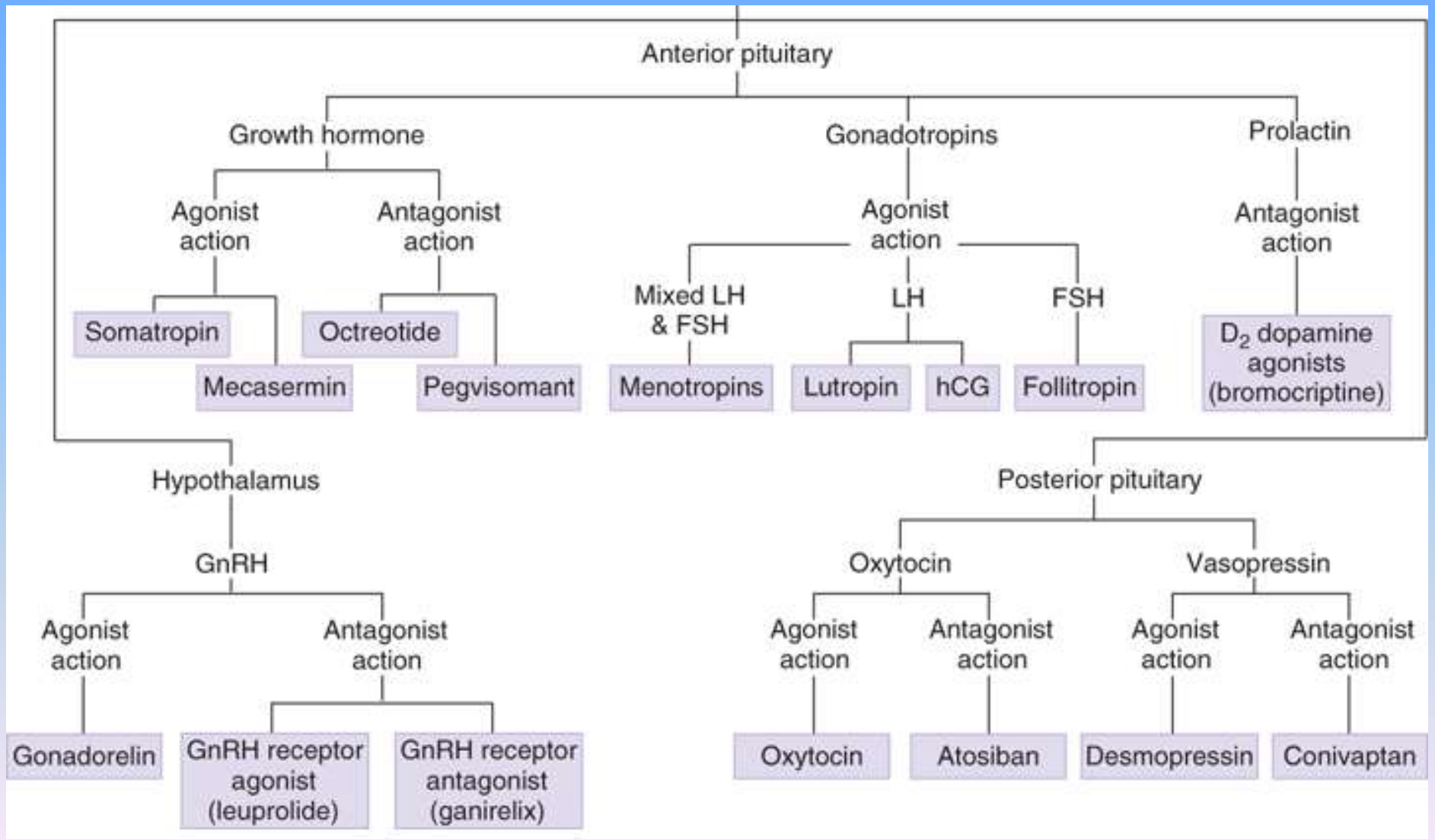
***Types of hormonal therapy*:**

- Replacement therapy – for hypofunction of endocrine gland (e.g.: insulin for diabetes mellitus)
- Patogenic therapy – for diseases unconnected with hormones deficit (e.g.: insulin for cachexia)
- Pharmacodynamic therapy is the usage of non-hormonal properties of hormones (e.g.: steroid Viadrilum for IV anesthesia)
- Stimulation therapy is the usage of hormones of anterior pituitary for stimulation of peripheral glands (e.g.: corticotropin after withdrawal of corticosteroids
- Antihormonal therapy is the usage of anti-hormones (e.g.: Mercasolylum for hyperthyroidism).

PRINCIPLES OF HORMONAL THERAPY

- Individual dose for each patient (e.g.: 1 IU of insulin for utilization of 3-5 g of sugar excreted with urine during a day)
- Taking into account of biological rhythms (e.g.: glucocorticoids are more effective in the morning when it's their peak concentration in the organism)
- Long-durative treatment (e.g.: insulin for type 1 diabetes mellitus)
- Gradual abolishing
- Stimulation therapy at the end of treatment (e.g.: corticotropin after the therapy by glucocorticoids).

DRUGS THAT MIMIC OR BLOCK EFFECTS OF HYPOTHALAMIC AND PITUITARY HORMONES



SOMATOSTATIN

- Somatostatin:14 amino acid peptide
- Produce mainly by hypothalamus and also in GIT
- Inhibits secretion of GH, TSH and prolactin by pituitary and insulin and glucagon by pancreas and all GIT secretions (Gastrin, HCl)
- All GIT secretions are inhibited including HCl - Diarrhoea, stetorrhoea, hypochlorhydria, nausea, dyspepsia etc. occurs
- Constrict hepatic, splanchnic and renal blood vessels
- **Uses:**
  - Acromegaly: limited use due to short half-life (2-3 min)
  - GI haemorrhages (250 mcg slow IV, 3 mg infusion for 12 Hrs)
  - Pancreatic, biliary and intestinal fistulae – antisecretory effects
  - APUD tumours producing excess HCl
  - Diabetic ketoacidosis (inhibits glucagon and GH secretion)
- **Drawbacks:** Short duration (2-3 min) and rebound GH secretion

NAFARELIN

- Long acting GnRH agonist and 150 times more potent than GnRH - Plasma half-life 2 -3 hrs
- Peak down regulation of pituitary GnRH receptors – 1 month
- **Uses:**
  - Assisted reproduction: 400 mcg BD intranasal followed by 200 mcg BD when Menstrual bleeding occurs For suppression of endogenous LH surge – matured oocyte can be harvested
  - Uterine fibroid: symptomatic relief 200 mcg BD
  - Endometriosis: 200 mcg for 6 months
  - Precocious puberty: 800 mcg BD nasal spray – arrest of breast and genital development
- Goserelin: Long acting – used as depot – Gn suppression, Ca Prostate, endometriosis etc. – 1-3 weeks earlier before ovulation
- Triptorelin – long acting (once a month): For regular release – daily SC injection (female infertility). For long-term use – IM injection monthly
- Leuprolide: Long acting IM/SC

PITUITARY HORMONES:
CLASSIFICATION

1. Anterior pituitary hormones and related substances

- Corticotropin
- Cosyntropin
- Somatotropin
- Human menopausal gonadotropin
- Human chorionic gonadotropin
- Prolactin
- Thyrotropin

2. Posterior pituitary hormones

- Oxytocin
- Vasopressin
- Desmopressin

3. Intermediate pituitary hormones

- Intermedin

PITUITARY HORMONES:
INDICATIONS

Corticotropin – hypofunction of adrenal cortex, after withdrawal of corticosteroids, rheumatism, collagenosis, bronchial asthma and severe allergy.

Somatotropin – insufficient secretion of growth hormone, pituitary dwarfness.

Thyreotropin – hypothyroidism, myxedema.

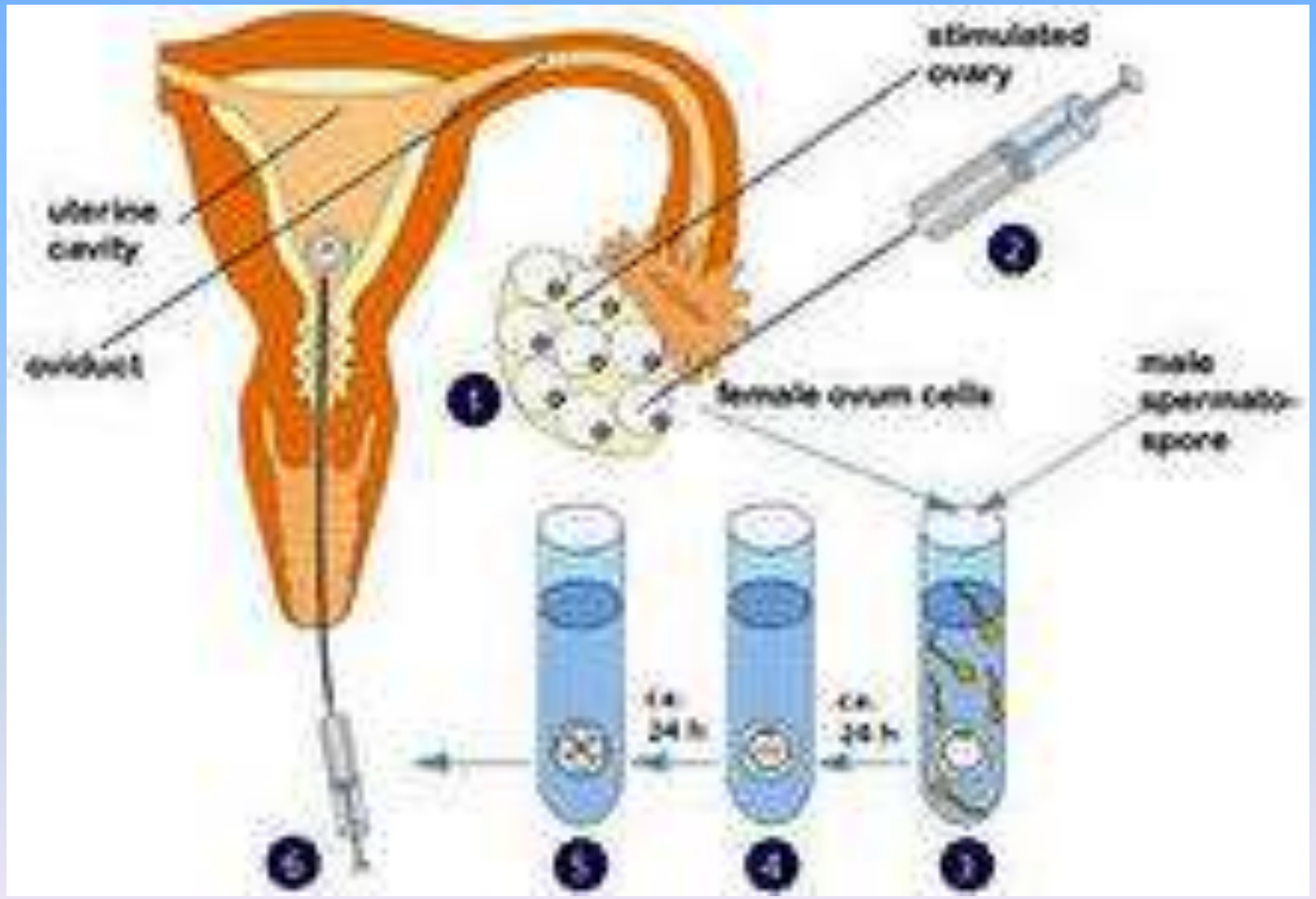
Human menopausal gonadotropin (hMG) and human chorionic gonadotropin (hCG) – hypogonadotropic hypogonadism, delayed puberty, ovulation dysfunction and sterility in women, hypospermia and sterility in men (hMG contains FSH and LH; hCG is LH agonist).

Oxytocin – weak labor activity, hypotonic metrorrhagia, promotion of milk ejection.

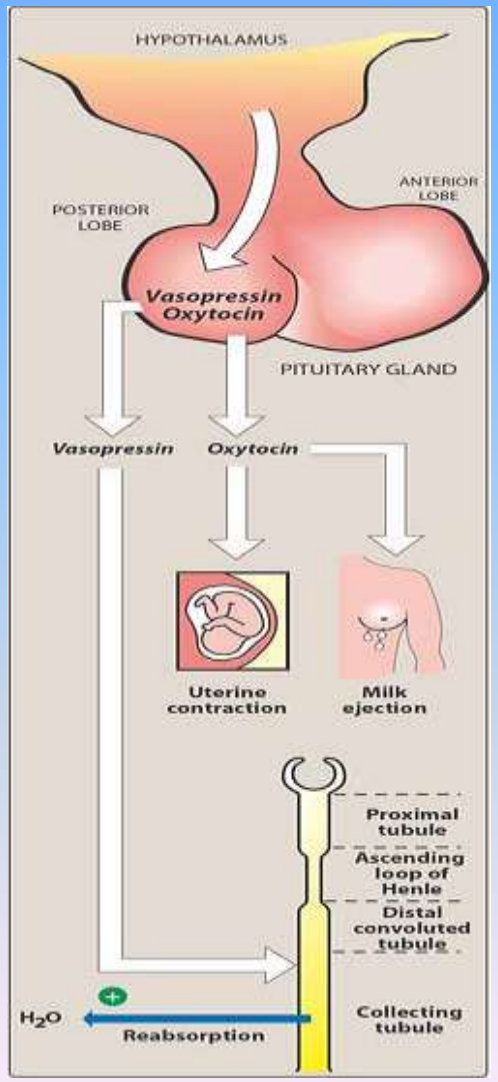
Adiurecrin (Vasopressin) – diabetes insipidus, shock, hemorrhage, hemophylia, atonia of the gut.

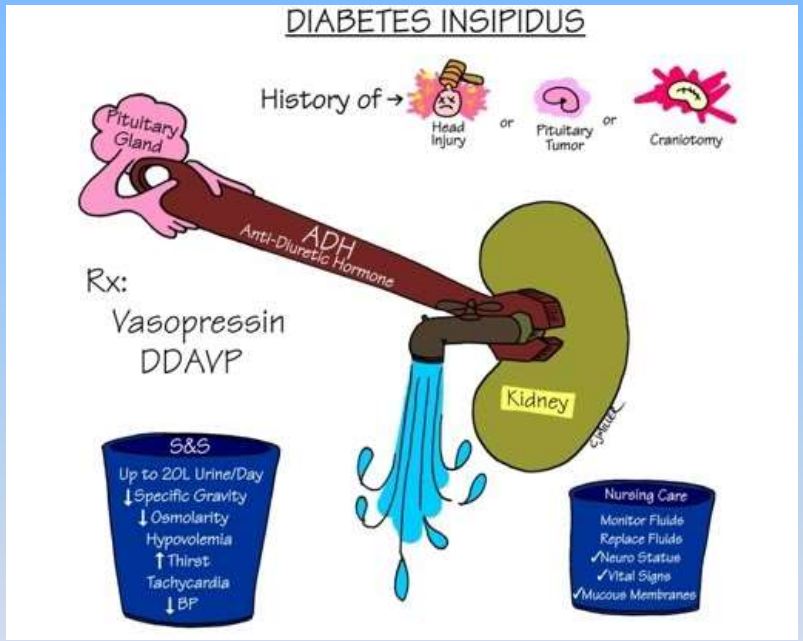
STH-RELATED CONDITIONS

GONADOTROPINS USE: IVF



PITUITARY HORMONES:
OXYTOCIN AND ADIURECRIN





THYROID AND ANTITHYROID DRUGS

CLASSIFICATION

1. Thyroid drugs

– Levothyroxine (L-thyroxine)

– α-Triiodthyronine hydrochloride

- Thyreocomb

2. Anti-thyroid drugs

– Methimazole (Mercazolilum)

- Thiamazole

– Iodides

HYPOTHYROIDISM

Iodine Deficiency Disorders

Goiter

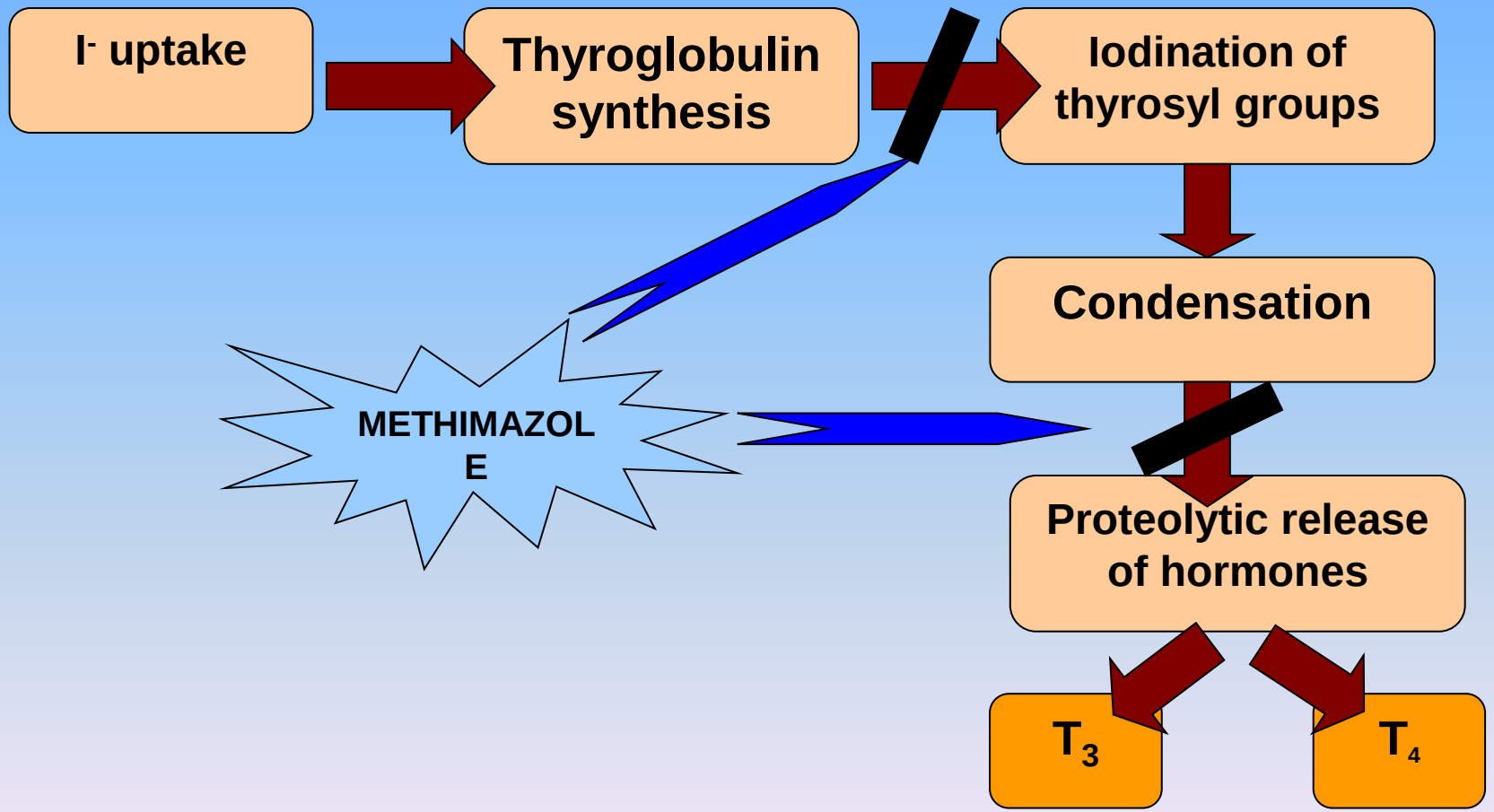
Cretinism

HYPERTHYROIDISM

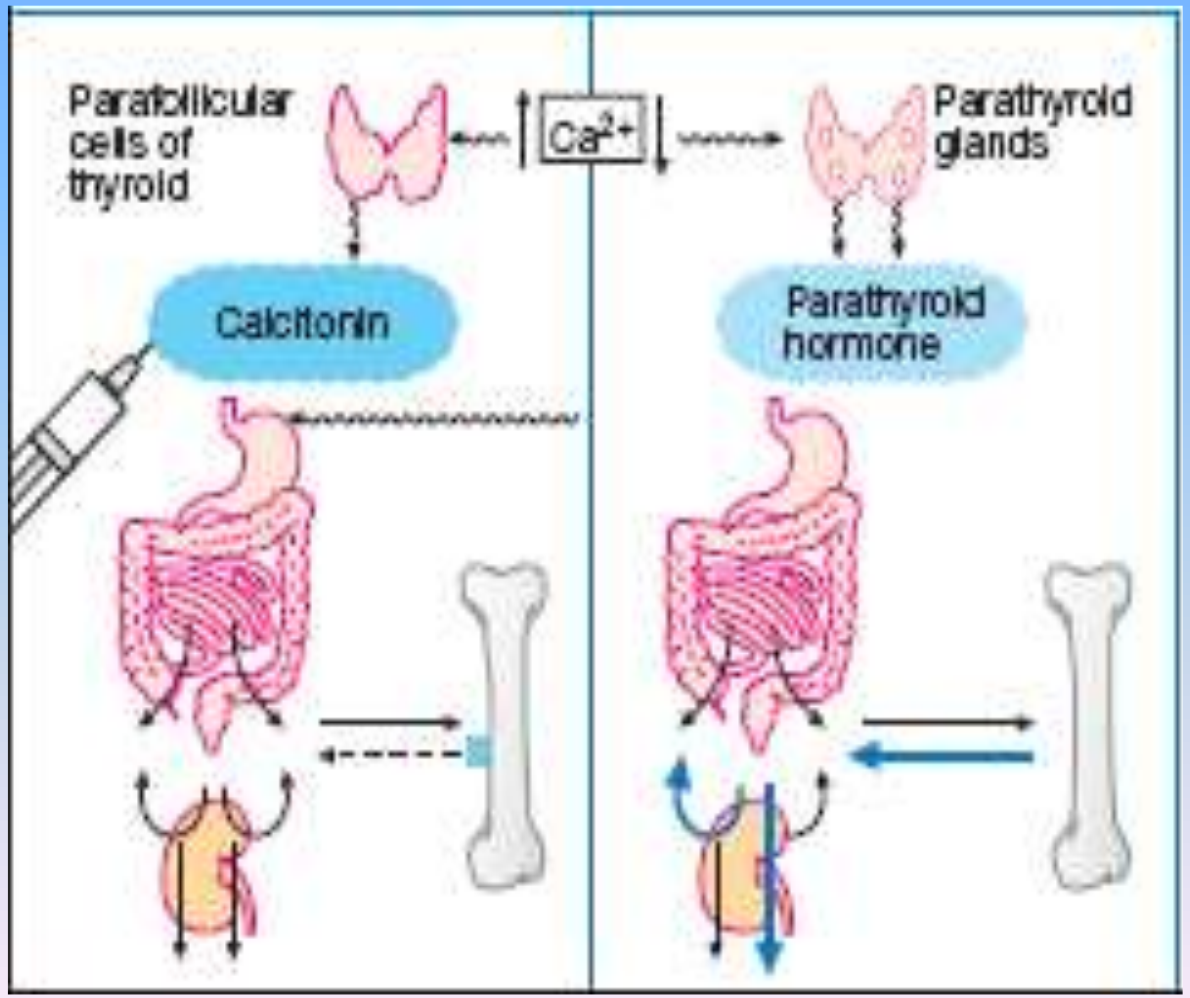
THYROID HORMONES:
PHARMACODYNAMICS AND INDICATIONS

PHARMACODYNAMICS	*INDICATIONS*
Increase in catabolism of proteins, lipids and carbohydrates Increase in basal metabolism Increase in body temperature Increase in activity of sympathetic nervous system Participation in growth and forming of mental faculties in children	Hypothyroidism (myxedema, cretinism) Diffuse non-toxic goiter Thyroiditis

ANTITHYROID DRUGS:
METHIMAZOLE (MERCAZOLILUM)



HORMONES REGULATING METABOLISM OF CALCIUM AND PHOSPHATE: EFFECTS



HORMONES REGULATING METABOLISM OF CALCIUM AND PHOSPHATE: INDICATIONS

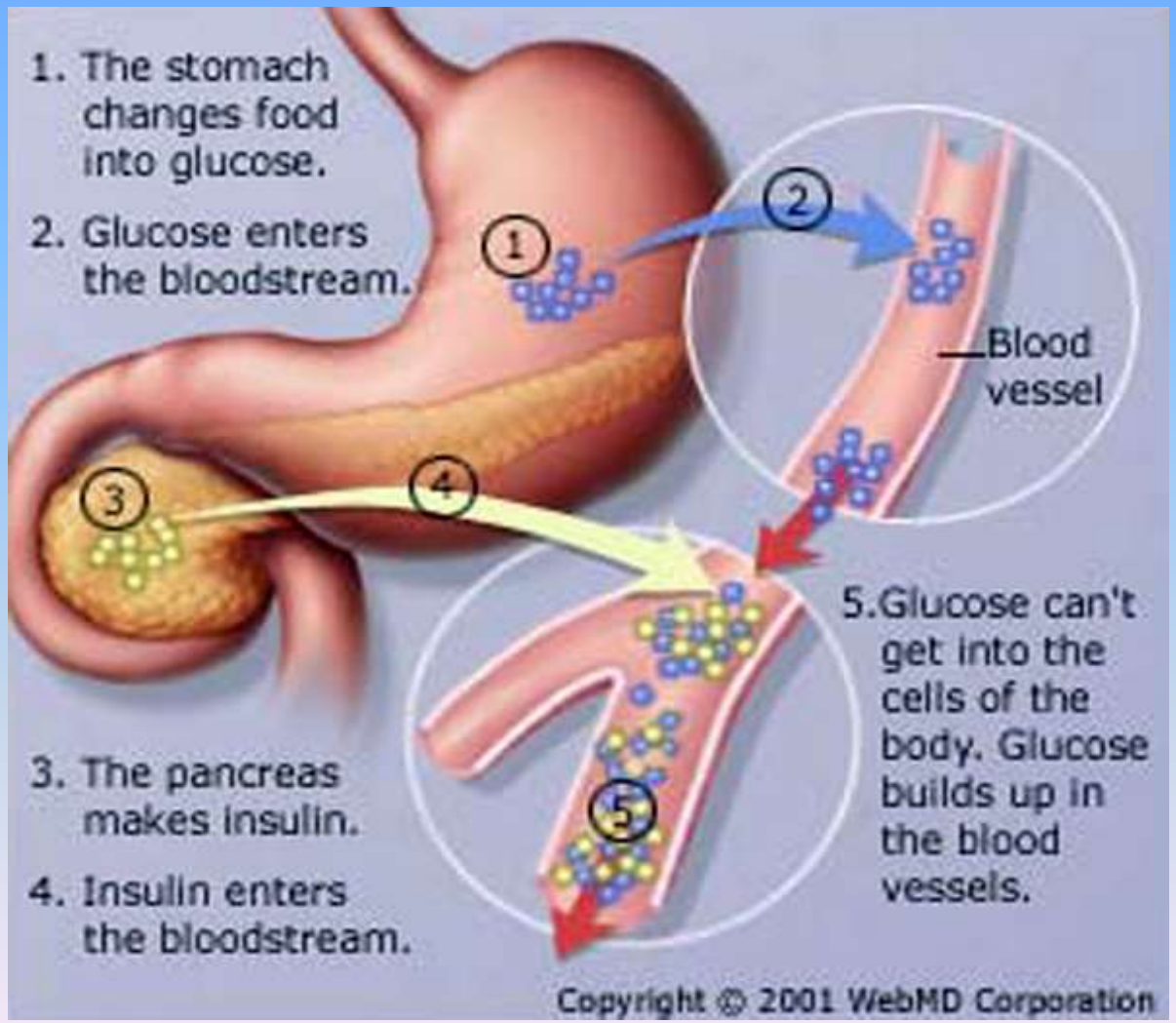
CALCITONIN (CALCITRINUM)	*PARATHYROIDIN*
Osteoporosis Padget's disease Bone fractures Bone pain in neoplastic malignant diseases Caries, severe paradontitis Hypercalcemia Nephrocalcinosis	Hypoparathyroidism (tetanus, spasmophylia) Allergic diseases

DIABETES MELLITUS

	Type 1	Type 2
Age of onset	Usually during childhood or puberty	Frequently over age 35
Nutritional status at time of onset	Frequently undernourished	Obesity usually present
Prevalence	5 to 10 percent of diagnosed diabetics	90 to 95 percent of diagnosed diabetics
Genetic predisposition	Moderate	Very strong
Defect or deficiency	β Cells are destroyed, eliminating the production of insulin	Inability of β cells to produce appropriate quantities of insulin; insulin resistance; other defects

DIABETES MELLITUS type 1

DIABETES MELLITUS type 2



ANTIDIABETIC DRUGS:
CLASSIFICATION

A. Insulin preparations

1. Rapid action preparations

– Regular insulin (Humalog, NovoRapid, Actrapid)

2. Prolonged action preparations

– Humulin

- Protafan

- Monotard

– Insulin glargine

B. Oral hypoglycemic agents

1. Sulfonylureas

– Chlorpropamide

– Glibenclamide

2. Biguanides

– Metformin

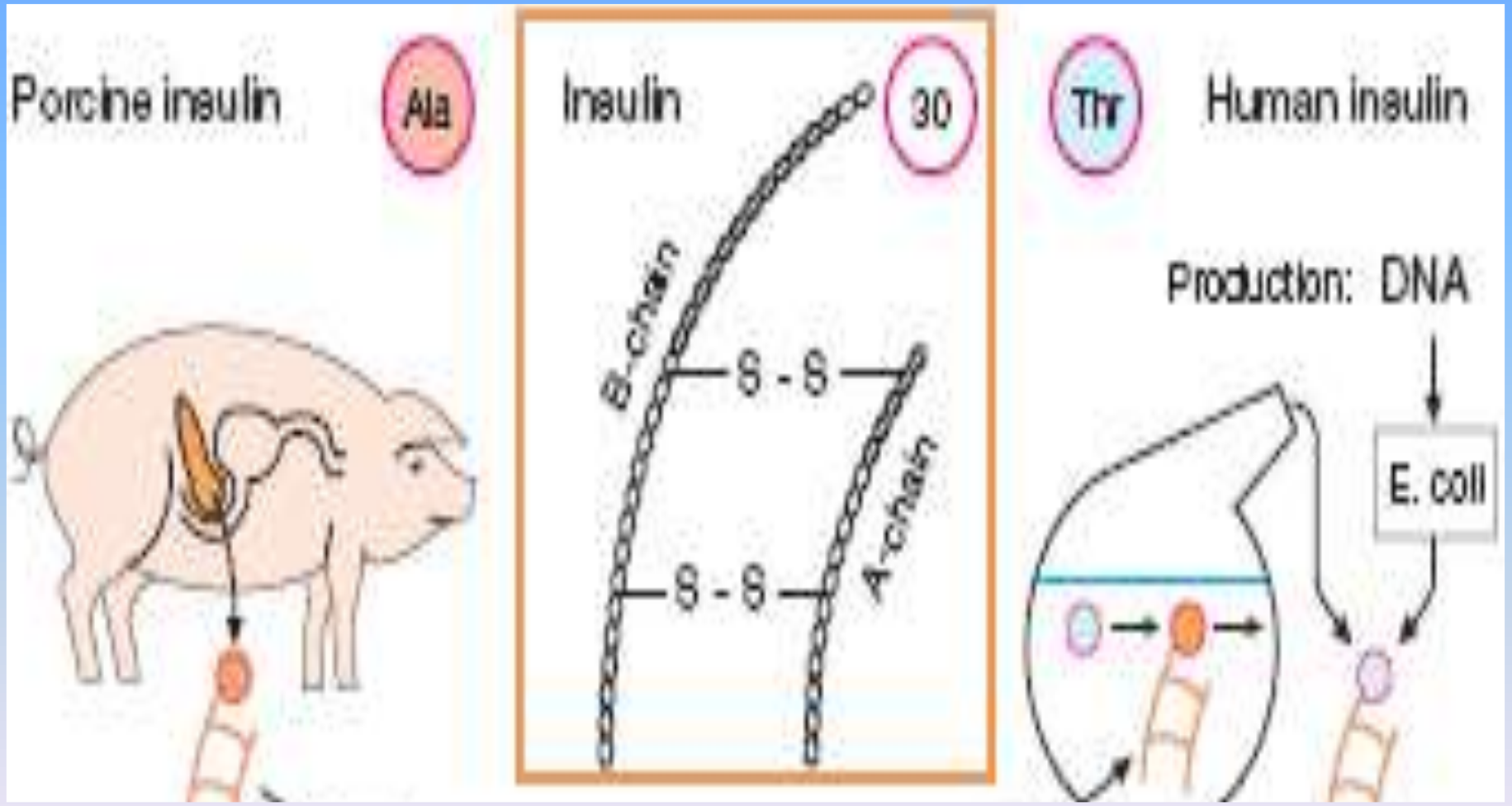
3. α-glucosidase inhibitors

– Acarbose

4. Thiazolidinediones

– Rosiglitazone

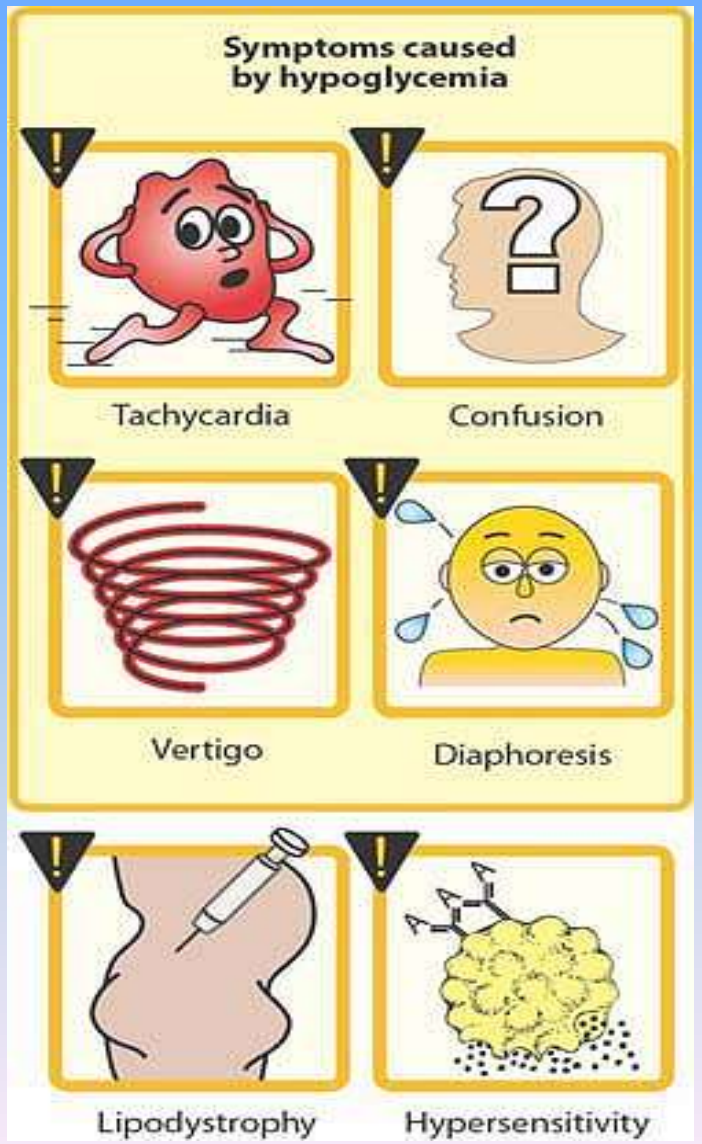
INSULIN:
CHEMICAL STRUCTURE AND SOURSES



INSULIN:
PHARMACODYNAMICS AND INDICATIONS

Pharmacodynamics	*Indications*
Increase in glucose entry into cells Decrease in gluconeogenesis Increase in utilization of glucose in the cells Increase in glycogen synthesis Increase in protein synthesisIncrease in cells proliferation (growth factor) Regulation of lipid metabolism Decrease in cetoacidosis	Diabetes mellitus (type 1) Diabetic (hyperglycemic) coma Cachexia Furunculosis Liver diseases Insulin-comatous therapy of schizophrenia For better availability of glucose during IV infusion

INSULIN:
SIDE EFFECTS



ORAL HYPOGLYCEMIC DRUGS:
PHARMACODYNAMICS

Sulfonylurea derivatives:

- increase of insulin release from the pancreas

Biguanides

- increase of glycolysis in tissues
- inhibition of hepatic gluconeogenesis
- decrease in glucose reabsorption in GI tract
- decrease in absorption of lipids in the gut and reduce of body weight
- lowering of hyperlipidemia.

α-glucosidase inhibitors

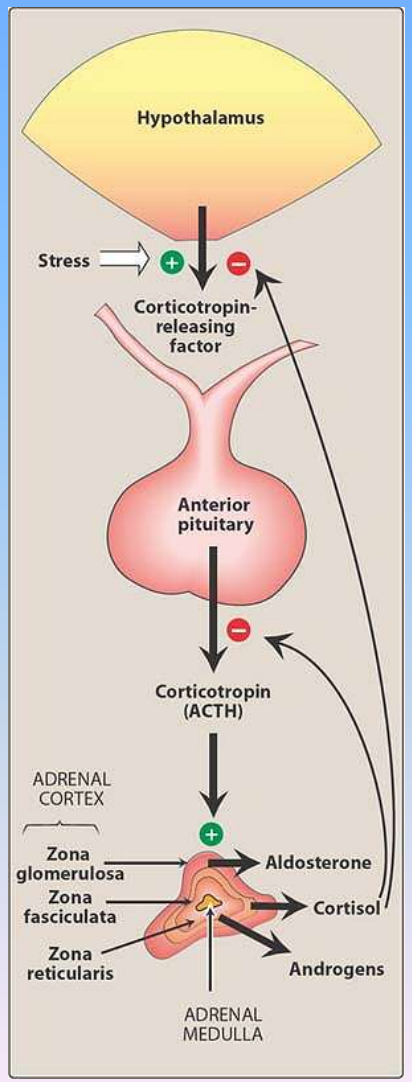
- competitive inhibition of a-glucosidase
- decrease monosaccharide absorption
- decrease blood sugar level

Thiazolidinediones

- increase tissue insulin sensitivity.

ORAL HYPOGLYCEMIC DRUGS:
SIDE EFFECTS

ADRENAL STEROIDS (CORTICOSTEROIDS)



ADRENAL STEROIDS (CORTICOSTEROIDS): CLASSIFICATION

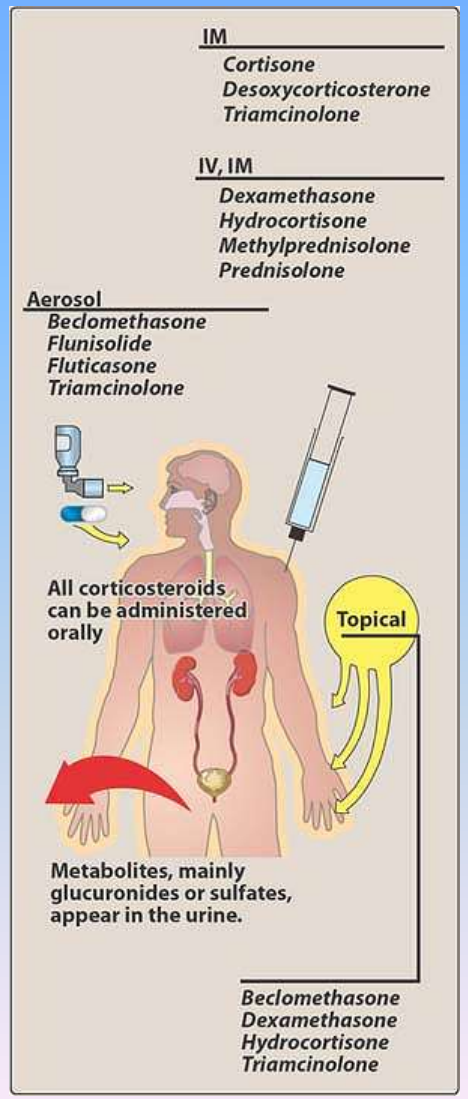
A. Glucocorticoids

1. Short-acting (8-12 hours)
– Hydrocortisone acetate
2. Intermediate-acting glucocorticoids (18-36 hours)
– Prednisolone
– Methylprednisolone
– Triamcinolone
3. Long-acting glucocorticoids (1-3 days)
– Dexamethasone
4. Topically active glucocorticoids
– Beclomethasone dipropionate
– Fluocinolone acetonide

B. Mineralocorticoids

– Desoxycorticosterone acetate.

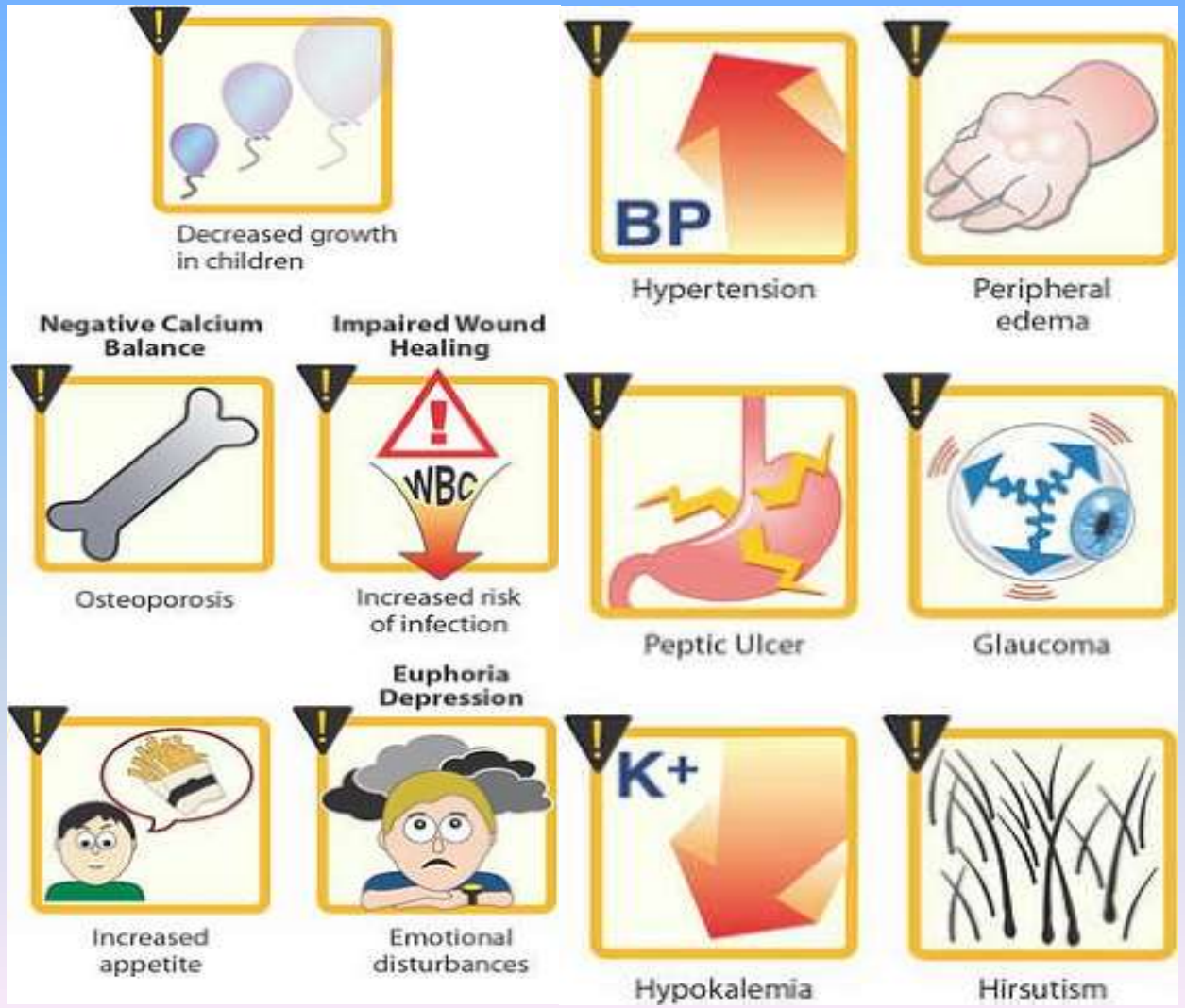
GLUCOCORTICOIDS:
PHARMACOKINETICS



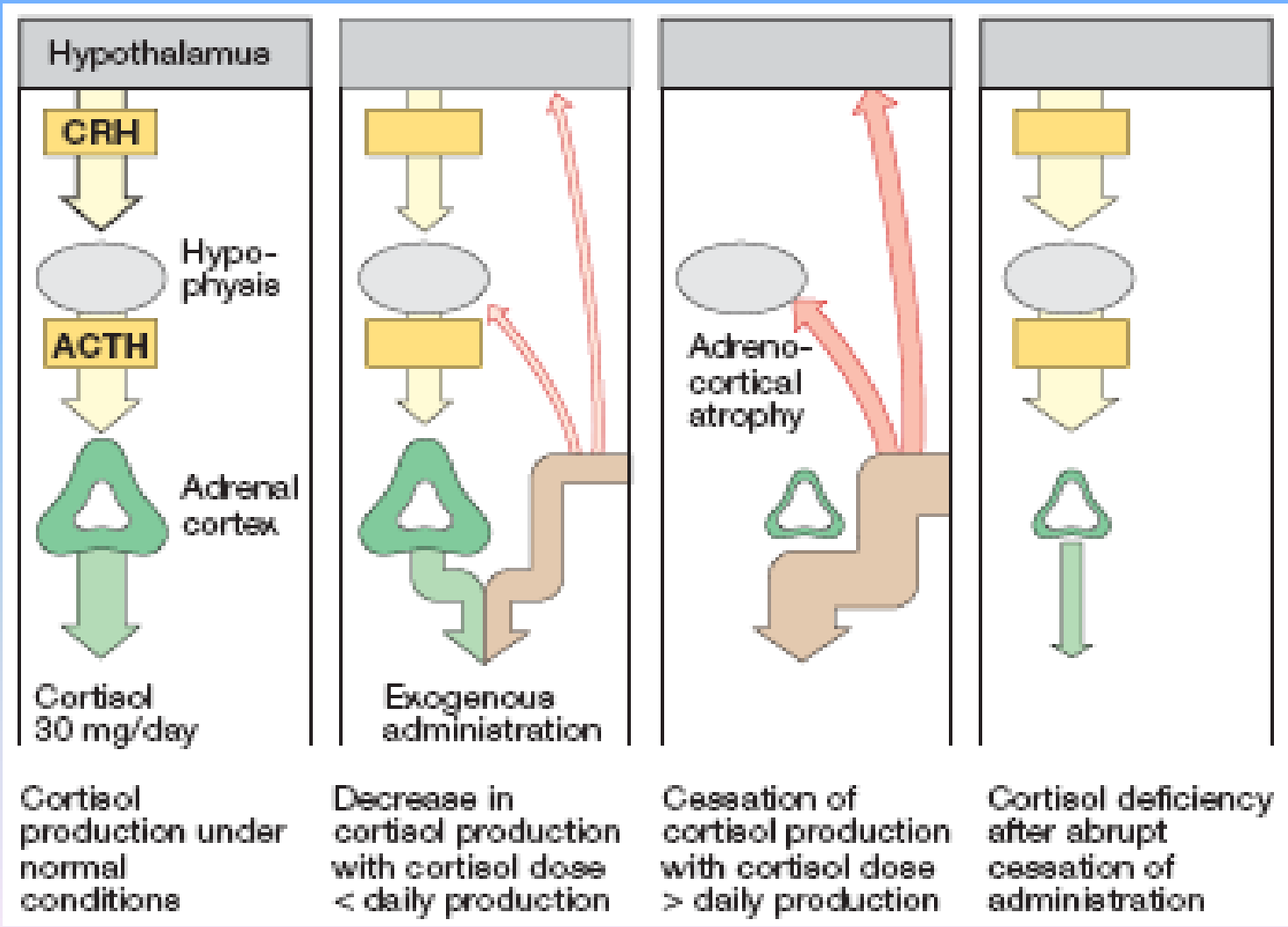
GLUCOCORTICOIDS:
PHARMACODYNAMICS AND INDICATIONS

PHARMACODYNAMICS	*INDICATIONS*
Increase in protein catabolism Increase in gluconeogenesis Increase in glucose level in blood Regulation of lipids distribution, increase in lipolysis Retention of sodium and water Increase in excretion of potassium and calcium Decrease in all phases of inflammation Suppression of immunity Oppression of allergic reactions Changes in blood film Inhibition of lymphoid tissue proliferation Increase in resistance to stress	Adrenal insufficiency Collagenosis, severe rheumatism Bronchial asthma Allergic diseases of skin and mucous membranes Autoimmune diseases Transplantation of organs Acute leukemia Shock Hypoglycemic coma Anaphylactic shock

GLUCOCORTICOIDS:
SIDE EFFECTS



GLUCOCORTICOIDS:
WITHDROWAL SYNDROME



MINERALCORTICOIDS:
DESOXYCORTICOSTERONE ACETATE

- is administered IM and sublingually
- regulates reabsorbtion of sodium, promotes retention of phosphate, calcium, carbonate, water and sodium
- supports BP and muscular tone
- is used to treat adrenocortical insufficiency and myastenia
- may cause edema, hypertension, hypokalemia.

GONADAL HORMONES:
CLASSIFICATION

A. *Male gonadal hormones and related substances*

1. Androgens
– Testosterone propionate
– Methyltestosterone
2. Antiandrogens
– Flutamid
3. Anabolic steroids
– Methandienone (Methandrostenolonum)
– Nandrolone phenyl propionate (Phenobolinum)
– Nandrolone deconoate (Retabolil)

B. *Female gonadal hormones and related substances*

1. Estrogens
– Estrone
– Synoestrol
– Diethylstilbestrol
2. Antiestrogens
– Tamoxifen citrate
3. Progestins
– Progesterone
– Allilestrnol
– Levonorgestrel
4. Antiprogestins
– Mifepristone

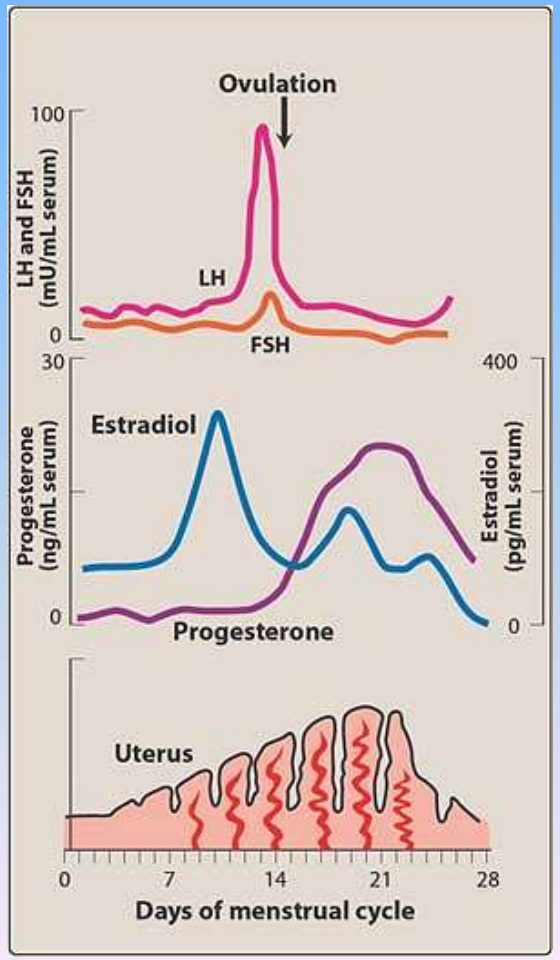
ANDROGENS:
TESTOSTERONE PROPIONATE

- is administered IM
- takes part in development of primary and secondary sex characteristics, maintains fertility in men; has anabolic action; maintains normal bone density
- is used to treat hypogonadism in men; also may be used in combined therapy of certain anemia, senile osteoporosis, severe burns, breast cancer in women before 60
- side-effects are masculinization in women, altered bone development in children, inhibition of gonadotropin release and reduction of spermatogenesis; gynecomastia in men, hepatitis, edema

ANABOLIC STEROIDS

PHARMACODYNAMICS	*INDICATIONS*
Increase in protein synthesis Retention of nitrogen, phosphor and calcium Stimulation of regeneration Increase in mass of skeletal muscles Increase in trophy of myocardium Decrease in glucose level in blood Increase in hemopoiesis	Cachexia Asthenia Wounds, ulcers Bone fractures, osteoporosis Ischemic heart disease Myopathy Diabetes mellitus (additional drug) Anemia (additional drug) Prolonged treatment with glucocorticoids

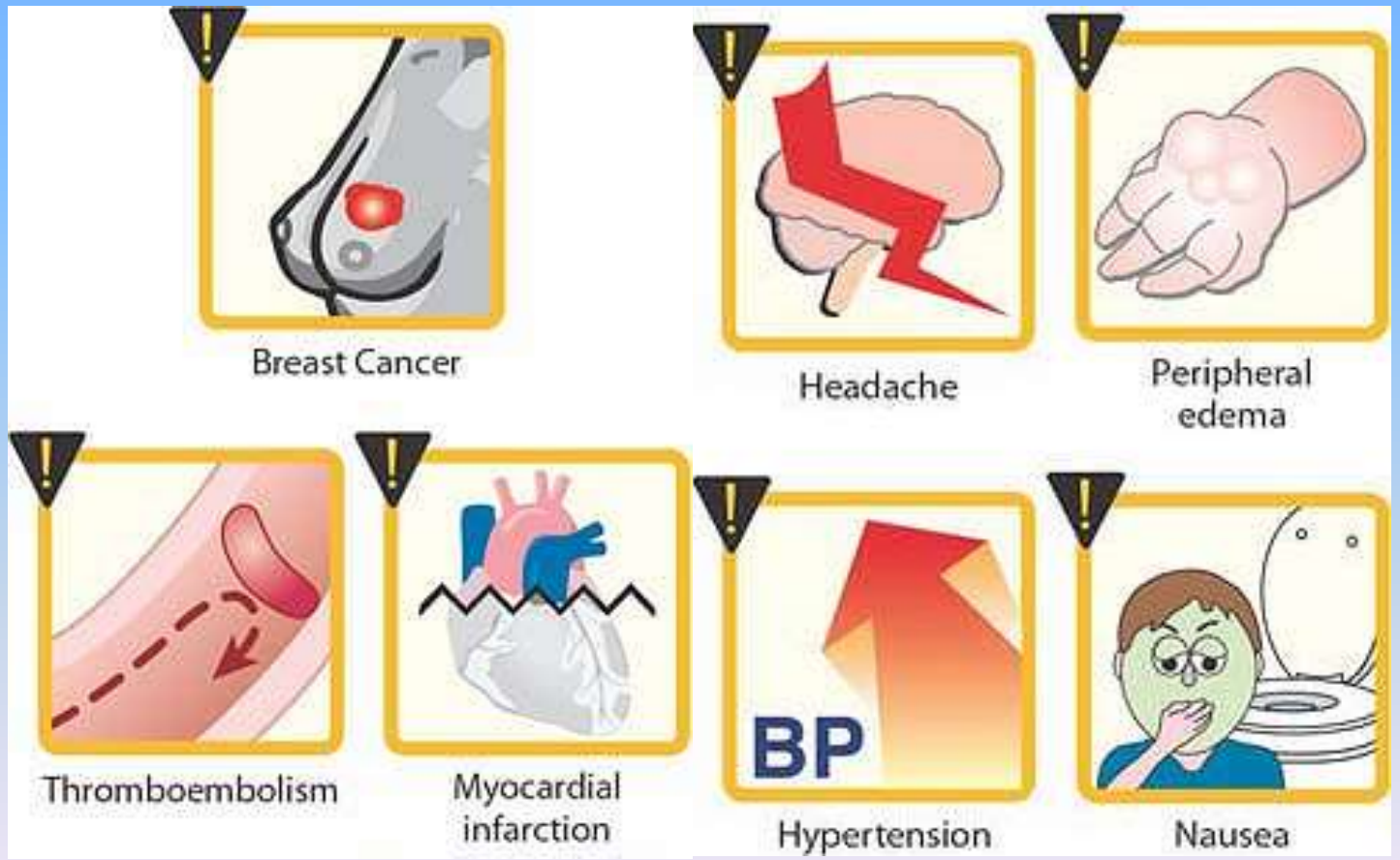
FEMALE GONADAL HORMONES:
ESTROGENS AND PROGESTINS



ESTROGENS:
ESTRONE (FOLLICULIN)

- is natural estrogen
- is administered IM, transdermally, vaginally; is metabolized in the liver and excreted with urine
- takes part in female sexual development, maintains the proliferation phase of menstrual cycle, increases uterus sensitivity to oxytocin and acetylcholine, has some metabolic effects (reduction of bone resorbtion, stimulation of calcium transport, reduction of cholesterol level in blood, increase in blood coagulation)
- is used for primary hypogonadism in young female, replacement therapy in menopause (postmenopausal hormone therapy), lack development of the ovaries or castration, for osteoporosis, stimulation of labor (together with oxytocin)
- side-effects: nausea, vomiting, edema, headache, hypertension, breast tenderness.

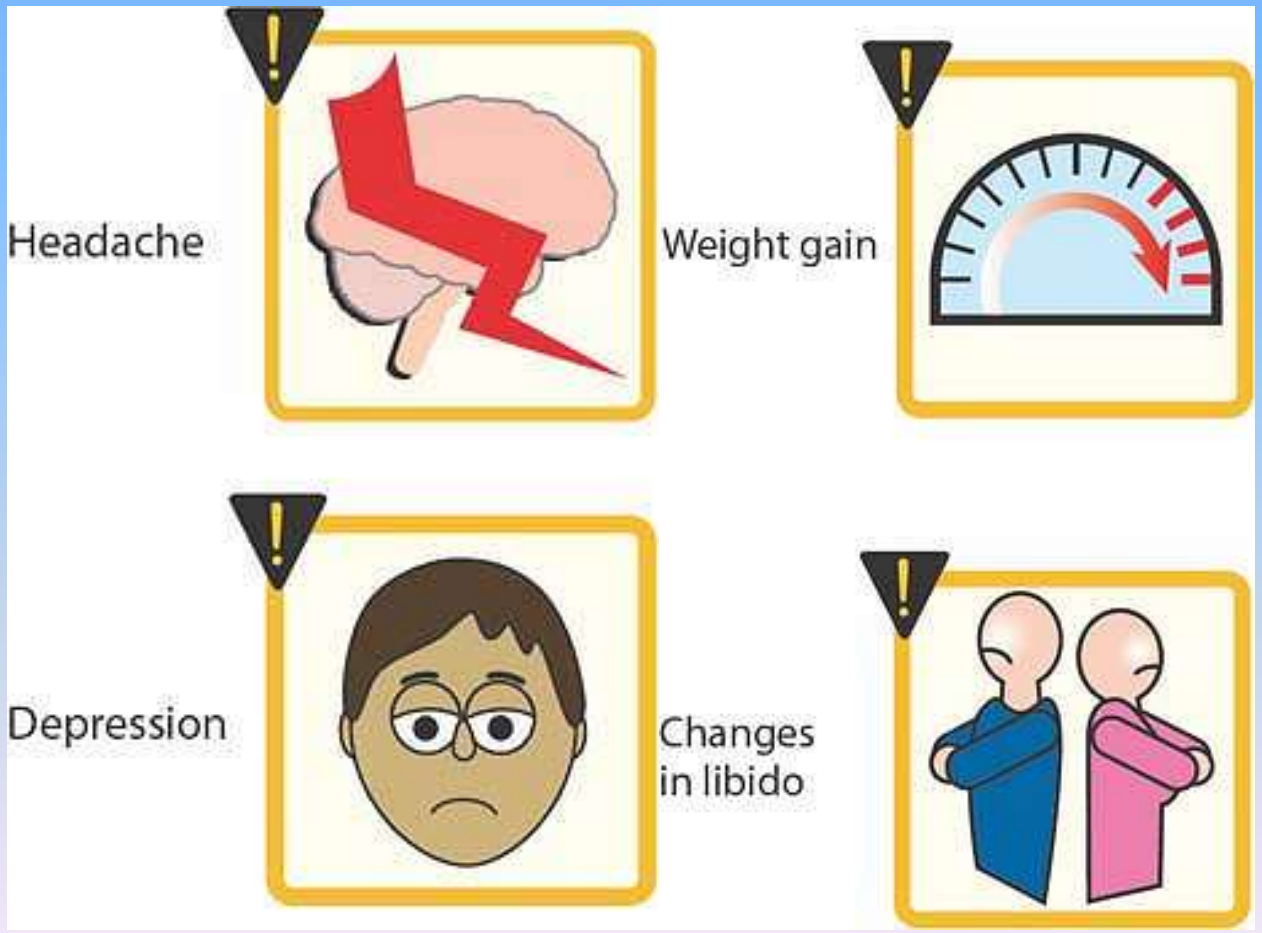
ESTROGENS:
ESTRONE'S SIDE EFFECTS



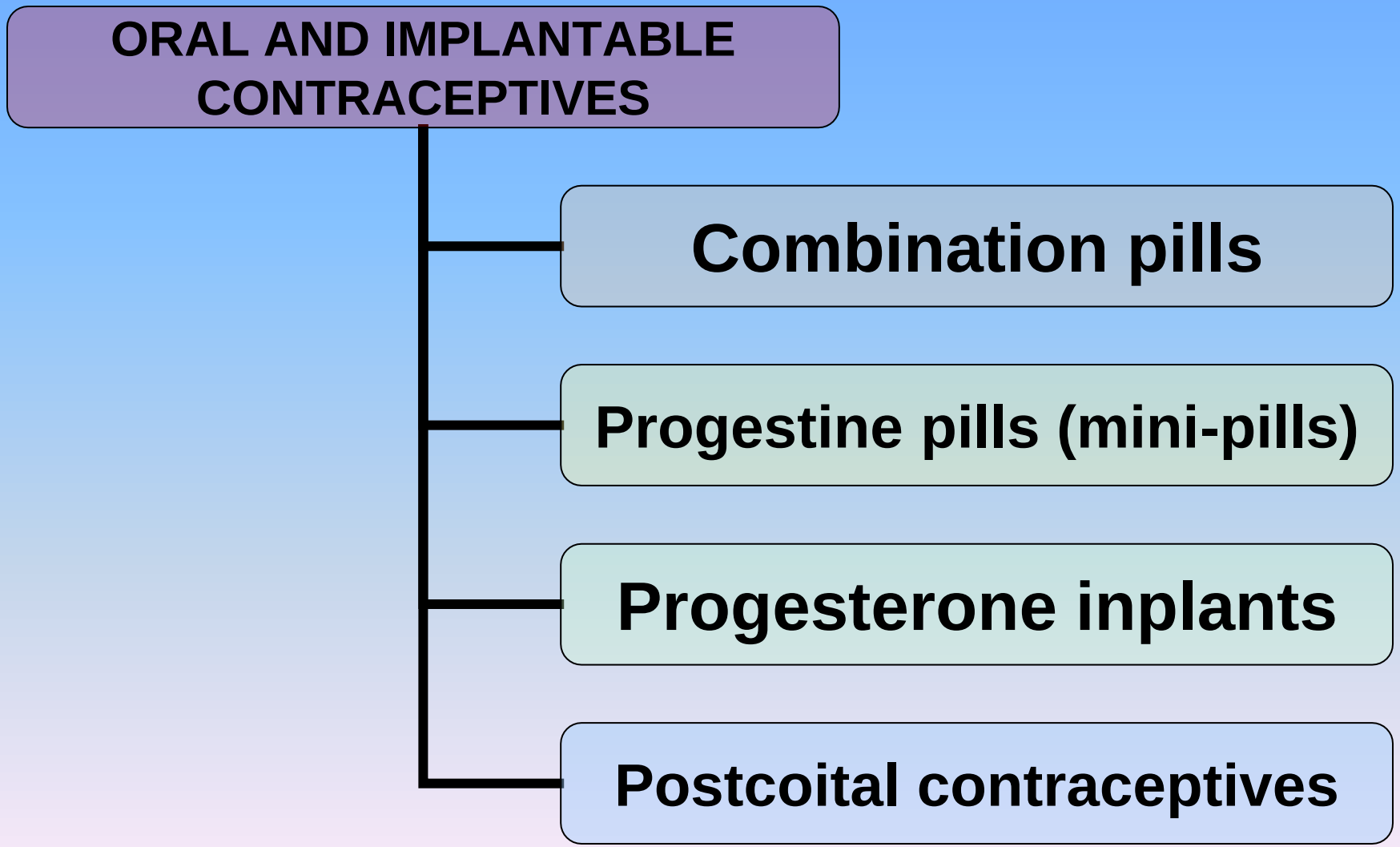
PROGESTINS:
PROGESTERONE

- is native progestin
- is given IM, but there are micronized form for oral administration and vaginal cream
- takes part in the development of sexual characteristics, maintains the luteal phase of menstrual cycle, stimulates maturation of uterus endometrium and provides implantation,. decreases uterus sensitivity to oxytocin and support normal development of pregnancy, promotes development of breast secretory tissue, acts on carbohydrate metabolism and stimulates fat deposition
- is used for prevention of spontaneous abortion, dysfunctional uterine bleeding, dysmenorrhea, endometriosis, suppression of postpartum lactation, endometrial carcinoma
- side-effects: uterine bleeding, dyspepsia, edema, depression, acne, hirsutism, weight gain

PROGESTINS:
PROGESTERONE'S SIDE EFFECTS



HORMONAL CONTRACEPTIVES
(DRUGS PREVENTING PREGNANCY)



CONTROL TASKS

- A patient has traumatic shock. Beside other measures, steroidal hormonal preparation is used for urgent treatment of this condition. What drug is mentioned?

A. Dexamethasone

B. Testosterone propionate

C. Clomiphene citrate

D. Progesterone

E. Finasteride. (A)

- Use of prednisolone ointment in the treatment of mycotic exema results in the generalization of infection. Which pharmacological effect of topically used glucocorticoid is a probable cause of this complication?

A. Anti-inflammatory

B. Anti-allergic

C. Catabolic

D. Immune suppressive

E. Hyperglycemic. (D)

CONTROL TASKS

- Tetany has developed after the thyreoidectomy. Using what drug is it possible to eliminate the problem?

A. Triiodothyroninum

B. Calcii chloridum

C. Parathyreoidinum

D. Calcitrinum.

E. Ergocalciferolum. (C)

- An old woman has osteoporosis complicated with hip bone fracture. She was prescribed with hormonal preparation from thyroid gland for improvement of bone mineralization. What drug is indicated to this patient?

A. Calcitrin

B. Parathyroidin

C. Thriiodthyronine

D. L-thyroxin

E. Regular insulin. (A)

CONTROL TASKS

- A patient has polyuria, polydipsia, and high level of glucose in the blood. The diagnosis is: Insulin dependent diabetes mellitus. Which hormonal preparation should be used for replacement therapy?

A. Regular insulin

B. Desmopressin

C. L-thyroxin

D. Thiamazole

E. Prednisolone. (A)

- A child has low growth, obesity, low body temperature, and retardation in the mental development. The diagnosis is: Hypothyroidism. Which hormonal preparation will be used for replacement therapy?

A. Actrapid

B. L-thyroxin

C. Gibenclamide

D. Glucagon

E. Metformin. (B)

THE END

Thank you for attention!