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PHARMACOLOGY

WORKBOOK

PART 1

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General pharmacology
Drugs acting on the peripheral nervous system
Drugs acting on the central nervous system
Drugs acting on the endocrine system

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III. DRUGS ACTING ON THE ENDOCRINE SYSTEM

UNIT 15

POLYPEPTIDE HORMONES AND RELATED DRUGS: HYPOTHALAMIC AND PITUITARY HORMONES AND THEIR SYNTHETIC ANALOGUES, DRUGS, REGULATING BONE MINERAL HOMEOSTASIS, INSULIN AND ORAL HYPOGLYCEMIC DRUGS. THYROID HORMONES AND ANTITHYROID DRUGS

1. TOPICS TO DISCUSS

1. Preparations of hypothalamic hormones and their synthetic analogues. Main uses in clinical practice.

2. The main pharmacological effects and therapeutic uses of octreotide.

3. Main functions of gonadotrophin-releasing hormone (GnRH). Therapeutic uses of preparations of synthetic GnRH and its analogues. Correlation between the administration regimen (pulsatile or continuous) and the hormone action.

4. Analogues of prolactin release-inhibiting factor (dopamine) and their main pharmacological effects. Main therapeutic uses of bromocriptine.

5. Preparations of anterior pituitary hormones and their synthetic analogues. Main uses in clinical practice.

6. Preparations of posterior pituitary hormones. Main effects of oxytocin and uses in clinical practice. The preparations of antidiuretic hormone and its synthetic analogues. Main difference between vasopressin and desmopressin.

7. Drugs regulating bone mineral homeostasis. The actions of parathormone, calcitonin and vitamin D_3 on calcium and phosphate turnover. Preparations of parathormone and calcitonin and their main therapeutic uses. Drugs used in the treatment of osteoporosis.

8. Thyroid hormones, their synthesis and major metabolic effects. Therapeutic uses of triiodthyronine and thyroxine in the treatment of hypothyroidism. Complications of the treatment. Antithyroid drugs, their mechanisms of action and therapeutic uses in different forms of hyperthyroidism. Main adverse effects.

9. Mechanisms of hypoglycemic action of insulin and its uses in the treatment of IDDM. Major hazards of insulin therapy.

10. The sources of insulin. Insulin preparations with different durations of action.

11. Oral hypoglycemic drugs: mechanisms of hypoglycemic action, therapeutic uses and adverse effects.

Background information

Polypeptide hormones

Polypeptide hormones are released by the hypothalamus, pituitary (anterior and posterior), the parathyroid glands (*PTH*), the thyroid gland (*calcitonin*), and the pancreas (*insulin*).

Hypothalamic hormones control the function of the anterior and posterior pituitary and therefore regulate secretion of pituitary hormones by stimulating (*releasing hormones*) or inhibiting it (*somatostatin, dopamine*).

Pituitary hormones released by the anterior pituitary specifically regulate the function of the peripheral endocrine glands and thus stimulate the secretion of certain hormones such as thyroxin, glucocorticoids, sex hormones, etc. They also control diverse metabolic processes and functions of different organs.

There are negative feedback pathways involved in regulation of hypothalamic and anterior pituitary hormone release:

- short pathway — anterior pituitary hormones inhibit the release of corresponding hypothalamic hormones;
- long pathway — hormones secreted by the peripheral endocrine glands inhibit the function of both the hypothalamus and the anterior pituitary. Therefore increased level of these hormones in the blood suppresses the release of hypothalamic and pituitary hormones and consequently the peripheral endocrine gland secretion.

2A. CLASSIFICATION OF HYPOTHALAMIC AND PITUITARY HORMONES AND RELATED DRUGS

Hypothalamic hormones	***Drugs***
Corticotropin-releasing hormone (CRH)	
Thyrotropin-releasing hormone (TRH)	Protireline
Growth hormone-releasing hormone (GHRH)	Sermorelin
Growth hormone release-inhibiting hormone (Somatostatin)	Octreotide
Gonadotrophin-releasing hormone (GnRH)	Gonadorelin, Leuprolide, Nafarelin, Goserelin
Prolactin release inhibiting factor (Dopamine)	Bromocriptine, Pergolide
Anterior pituitary hormones	***Drugs***
Corticotropin (ACTH)	Cosyntropin (Tetracosactide)
Thyrotropin (TSH)	Thyrotropin alpha (rhTSH)
Growth hormone (Somatotropin)	Somatropin, Somatrem
Gonadotropins	Human menopausal gonadotrophin (hMG, Menotropins), Urofollitropin (uFSH), Follitropin (rFSH), Human chorionic gonadotrophin (hCG)
Posterior pituitary hormones	***Drugs***
Oxytocin	Oxytocin
Antidiuretic hormone (ADH)	Vasopressin, Lypressin, Desmopressin, Terlipressin

Background information

Hormone release-inhibiting hormones

Secretion of growth hormone is decreased by somatostatin and dopamine. Therefore a long-acting analogue of somatostatin - *octreotide* and dopamine agonists such as *bromocriptine* are used in the management of acromegaly (the condition associated with hypersecretion of growth hormone in adults leading to enlargement of hands, feet and facial structures).

Somatostatin also inhibits the release of thyrotropin, insulin, glucagon, and most gastrointestinal hormones. This allows the use of octreotide in hormone-secreting tumors.

Dopamine exerts inhibitory control on prolactin release that allows the use of the agonist of dopamine receptors, *bromocriptine,* in the treatment of galactorrhea and prolactin-secreting pituitary tumors.

Gonadotrophin- releasing hormone (GnRH) stimulates gonadotrophin release and induces ovulation given in pulsatile fashion to mimic its physiological secretion. The synthetic preparation of GnRH termed *gonadorelin* is used in pulsatile fashion to treat infertility caused by hypogonadism.

But when given continuously GnRH inhibits gonadotrophin release that results from down-regulation or desensitization of the GnRH receptors on the pituitary cell membranes. To reach this effect potent analogues of GnRH (leuprolide and others) are used continuously by nasal spray or s/c depot preparation in the treatment of sex hormone-dependent disorders (prostate or breast cancer, endometriosis and precocious puberty).

Gonadotropin production is also decreased by *cetrorelix*, an antagonist of GnRH receptors and *danazol*, a partial agonist of progestogen and androgen receptors. The decreased production of gonadotropin stimulates the negative feedback effect on the hypothalamus and the anterior pituitary. Estrogen synthesis in the ovary is reduced resulting in the decrease of endometrial proliferation. *Danazol* and cetrorelix are used in endometriosis (condition associated with growth of endometrial tissue outside the uterine cavity).

Background information

Antidiuretic hormone

Polypeptide hormones interact with G-protein coupled receptors on the cell membranes. Receptors for ADH (*vasopressin*) are located on the cells of distal renal tubules and collecting duct (V_2-receptors coupled to adenylate cyclase) and on vascular smooth muscle cells (V_1-receptors coupled to phospholypase C). Acting on V_2-receptors vasopressin increases water reabsorption by increasing the number of water channels in the tubular luminal membranes. In higher doses vasopressin acts on V_1-receptors that results in vasoconstriction. Vasopressin also promotes release of ACTH from the anterior pituitary by an action on V_3-receptors.

Background information

The states of thyroid dysfunctions:

– hyperthyroidism *(thyrotoxicosis)* is associated with excessive blood level and activity of thyroid hormones. The main symptoms are high metabolic rate, tachycardia, tremor, nervousness, sweating, an increase of skin temperature, increased appetite with loss of weight etc.

– hypothyroidism *(myxoedema* — in adults*)* is characterized by low metabolic rate, slow speech, bradycardia, lethargy, mental impairment, thickening of the skin and some other symptoms which are associated with low level of thyroid hormones. The main form of hypothyroidism is Hashimoto's thyroiditis, a chronic autoimmune disease caused by formation of antibodies against thyroglobulin or some other components of the thyroid tissue. Congenital disturbances in the development of the thyroid gland in children result in growth retardation and mental insufficiency *(cretinism)*.

– simple non-toxic goitre may be associated with dietary iodine deficiency. Increase of TRH and TSH release (due to cessation of negative feedback effect when the level of thyroid hormones is too low) results in increase of the thyroid gland size. Small amount of iodide (150 – 300 μg/day) in the form of iodized table salt is required for the treatment of this condition. Similar condition may be caused by *antithyroid drugs* (e.g.thioamides).

Background information

Treatment of hyperthyroidism

There are several types of hyperthyroidism among which two are common.

Diffuse toxic goitre (Graves' isease) is an autoimmune disorder. Thyroid overactivity is caused by the formation of IgG antibodies that bind to and activate TSH receptors. Initial treatment consists in reversible suppression of thyroid overactivity by means of a*ntithyroid drugs.*

Toxic nodular goitre is associated with benign hormone-producing adenoma. The preferred treatment is surgical removal or administration of *radioiodine (iodine- 131)* which is taken up by the thyroid gland. Being incorporated into thyroglobulin it causes restricted destruction of cells of thyroid follicles by emitting β-particles. Cytotoxic effect on the gland lasts 1-2 months after a single dose.

Antithyroid drugs

1. Thioamides (thiourea derivatives, thiourelenes): *thiamazole* (*methimazole), propylthiouracil*

2. *Iodine in high dosage* causes shorter-lasting and more rapid effect than thioamides. Iodine solution in potassium iodide (*Lugol's iodine*: 5%J + 10%KJ) is recommended for rapid thyroid suppression in thyrotoxic crisis.

3. β-*Blocking drugs (propranolol* and rapidly acting *esmolol)* reduce the symptoms of thyrotoxicosis such as tacycardia, tremor, sweating etc.

4. *Radioiodine (*in toxic nodular goitre*)*

Background information

Regulation of bone mineral homeostasis

Hormones released by the parathyroid glands (*parathormone*; *PTH*) and by "C" cells of thyroid gland follicles *(calcitonin)* regulate metabolism of calcium and phosphate acting inversely on turnover of calcium.

PTH increases concentration of Ca^{2+} in the blood by mobilizing it from bone. Besides PTH decreases excretion of Ca^{2+} and increases excretion of phosphate by the kidney.

Calcitonin decreases plasma Ca^{2+} concentration increasing its concentration in bone and thus prevents osteopenia (reduction in the bone mineral content) and inhibits bone resorption. This allows to use calcitonin in the treatment of osteoporosis

Osteoporosis is the disease characterized by reduction of bone mass with distortion of microarchitecture of the bone resulting in increased risk of fractures.

Bone homeostasis is maintained by dynamic balance between anabolic (bone formation) and catabolic (bone resorption) processes. Osteoporosis develops when balance shifts in favor of bone resorption and calcium is mobilized from the bone rather than deposited as hydrohyapatites. The common causes of osteoporosis are age-related such as estrogen deficiency in postmenopause. Treatment with glucocorticoids, thyroxin and long-term immobilization also can lead to osteoporosis.

2B. CLASSIFICATION OF DRUGS USED IN THE TREATMENT OF OSTEOPOROSIS

I. Drugs which decrease bone resorption

– bisphosphonates*: alendronate, pamidronate*
– calcitonin (*salmon calcitonin, salcatonin*)
– postmenopausal replacement therapy (*estrogen* + *progestin, raloxifene* (see unit 16)

II. Drugs which increase bone formation

– PTH in low doses (PTH 1-34 fragment called *teriparatide*)
– fluoride
– anabolic steroids (see unit 16)

III. Drugs which are essential for bone mineralization

– calcium salts: *calcium gluconate, calcium carbonate*
– vitamin D preparations: *calcifediol, calcitriol.*

Background information

Types of diabetes mellitus

Diabetes mellitus is a chronic metabolic disorder characterized by an elevation of blood glucose level caused by a relative or absolute deficiency of insulin.

Absolute deficiency of insulin mainly results from autoimmune destruction of B-cells of pancreatic islets. This condition is called type 1 or insulin-dependent diabetes mellitus (IDDM) and requires replacement administration of insulin.

Relative deficiency of insulin mostly results from progressive decline of β-cells function with age and is accompanied by insulin resistance (decreased sensitivity of target cells to insulin). This condition is called type 2 or non-insulin-dependent diabetes mellitus (NIDDM). The treatment of this form of diabetes may be initially dietary but oral hypoglycemic drugs are usually required for normalization of blood glucose level. Many patients ultimately require replacement therapy with insulin.

Preparations of insulin are classified according to its origin into human and porcine. Besides recombinant forms of human insulin are now available.

Note: The most important problem in insulin therapy is to avoid fluctuations in plasma concentration of insulin and thus in blood glucose level. This problem is tried to be solved by using insulin preparations varying in the timing of peak concentration and duration of action.

Preparations of insulin according to the rate of onset and duration of action

A. Rapid-acting preparations:

a. Regular (crystalline zinc) insulin is available in the form of clear neutral solution for IV (emergencies) and s.c. use.

b. Semilente insulin (insulin zinc suspension) for s/c use.

c. Insulin analogues (Lispro, Aspart, Glulisine) are obtained from human insulin by replacement of some amino acids that results in faster absorption from the site of s.c. injection. That is why insulin analogues must be used immediately before meal (regular insulin must be injected 30 minutes before meal). Based on this priperty they are called ultra-rapid.

B. Intermediate-acting preparations:

a. Isophane insulin (NPH insulin) is a suspension of insulin in a complex with zinc and protamine.

b. Lente insulin (insulin zinc suspension) is a mixture of ultralente and semilente insulins.

C. Long-acting preparations:

Ultralente insulin (extended insulin zinc suspension) has a slower onset of action and provides a low basal concentration of insulin during a day.

Insulin analogue glargine is produced from human insulin by modifications in structure that enhances its stability. Given s.c. once-daily it provides more constant basal level of insulin during 24 hours than ultralente insulin due to prolonged absorption from the site of injection.

2C. CLASSIFICATION OF ORAL HYPOGLYCEMIC DRUGS

Sulfonylureas:

First generation: *Chlorpropamide, Tolbutamide*

Second generation: *Glimepiride, Glipizide, Glibenclamide (glyburide), Gliclazide*

Meglitinides: *Nateglinide, Repaglinide*

Thiazolidinediones: *Pioglitazone, Rosiglitazone*

Biguanides: *Metformin*

Alpha-glucosidase inhibitors: *Acarbose, Miglitol*

Background information

Oral hypoglycemic drugs

Insulin secretagogues: *sulfonylureas* and *meglitinides* resemble the action of physiological secretagogues such as glucose. The major side effect of these drugs is hypoglycemia (less with nateglinide). The main difference between sulfonylureas and meglitinides concerns the rate of absorption and elimination. Meglitinides are more rapidly acting and shorter acting drugs. Given shortly before meal they reduce postprandial rise in glucose level that is not adequately controlled by sulfonylureas. The action of *nateglinide* on insulin secretion depends on blood glucose level (the lower glucose level – the less effect of nateglinide) therefore it is unlikely to affect fasting glucose level.

Insulin sensitizers: thiazolidinediones decrease insulin resistance and enhance insulin action in target tissues. They bind to and activate nuclear peroxisome proliferator-activated receptor-gamma (PPAR-gamma) and thus promote transcription of insulin-responsive genes. This increases insulin signaling including synthesis and translocation of specific glucose transporter GLUT4 that facilitates the movement of glucose into the skeletal muscle and adipose tissue cells. Thiazolidinediones exert their effect only in the presence of insulin thus increasing effectiveness of endogenous insulin action.

3. MULTIPLE CHOICE QUESTIONS

1. Which of the following drugs are preparations of hypothalamic hormones or their analogues?
1. Octreotide
2. Leuprolide
3. Menotropins
4. Sermorelin
5. Somatrem
6. Protireline
7. Desmopressin

2. Which of the following drugs are preparations of anterior pituitary hormones or their analogues?
1. Octreotide
2. Leuprolide
3. Somatrem
4. Sermorelin
5. Menotropins
6. Protireline
7. Desmopressin

3. Which of the following drugs are preparations of posterior pituitary hormones or their analogues?
1. Oxytocin
2. Leuprolide
3. Somatropin
4. Sermorelin
5. Protireline
6. Desmopressin

4. All of the following statements about the adrenocorticotropic hormone are true, EXCEPT:
1. Adrenocorticotropic hormone is also called corticotrophin.
2. It stimulates the synthesis and release of corticosteroids.
3. Release of adrenocorticotropic hormone can be inhibited by cortisol.
4. It is more useful clinically than glucocorticoids.
5. Its main clinical use is as a diagnostic test.

5. Peptide with ACTH (adrenocorticotrophin)-like properties is which of the following?
1. Cosyntropin
2. Bromocriptine
3. Somatomedin
4. Somatrem
5. Octreotide

6. The main indication of cosyntrophin (tetracosactrin) is which of the following?
1. Diagnosis of adrenal cortical insufficiency
2. Autoimmune diseases
3. Bronchial asthma

7. Cosyntrophin in comparison with corticotrophin:
1. is less immunogenic
2. provokes antibody formation to more extent.

8. Which of the following drugs is used as a diagnostic test for growth hormone secretion?
1. Octreotide
2. Leuprolide
3. Protireline
4. Sermorelin
5. Somatrem

9. Which of the following drugs is a long-acting analogue of somatostatin?
1. Octreotide
2. Leuprolide
3. Desmopressin
4. Sermorelin
5. Somatrem

10. All of the following statements concerning octreotide are correct, EXCEPT:
1. It is more potent than somatostatin in inhibiting growth hormone release.

2. It is relatively less potent in reducing insulin secretion than in reducing growth hormone release.
3. If compared with somatostatin it rarely causes hyperglycemia.
4. It decreases the release of most gastrointestinal hormones.
5. It stimulates gastric acid and pancreatic secretion.

11. Which of the following are therapeutic uses of octreotide?
1. Control of bleeding from oesophageal varices
2. Treatment of acromegaly
3. Diagnosis of endocrine insufficiency
4. Control of hormone-secreting tumors
5. Growth hormone deficiency

12. Which of the following factors stimulate growth hormone secretion?
1. Growth hormone-releasing hormone
2. Somatostatin
3. Somatomedins
4. Deep sleep, especially in children

13. Which of the following are preparations of growth hormone in clinical use?
1. Octreotide
2. Leuprolide
3. Somatropin
4. Sermorelin
5. Somatrem

14. Which of the following statements concerning insuline-like growth factors (IGFs, somatomedins) are correct?
1. They stimulate growth hormone secretion.
2. They are peptides which mediate the action of growth hormone.
3. Growth hormone stimulates synthesis of these peptides.
4. IGF-1 inhibits growth hormone secretion.
5. IGF-1 inhibits somatostatin release from the hypothalamus.

15. The effects of growth hormone are all of the following, EXCEPT:
1. Stimulation of IGFs production
2. Decrease of sulfate uptake into cartilage
3. Increase of amino acid uptake by the cells
4. Stimulation of protein synthesis
5. Increase of bone growth.

16. Which of the following drugs can be used in short stature caused by growth hormone deficiency?
1. Octreotide
2. Bromocriptine
3. Somatropin
4. Sermorelin
5. Somatrem

17. Which of the following drugs can be used to suppress high level of growth hormone in acromegaly?
1. Octreotide
2. Leuprolide
3. Protireline
4. Sermorelin
5. Bromocriptine

18. Prolactin release-inhibiting factor is considered to be which of the following?
1. Somatostatin
2. Sermorelin
3. Protireline
4. Dopamine
5. Menotropins

19. Which of the following drugs can be used to suppress prolactin secretion?
1. Octreotide
2. Pergolide
3. Protireline
4. Sermorelin
5. Bromocriptine

20. The therapeutic uses of bromocriptine are all of the following, EXCEPT:
1. Acromegaly
2. To increase lactation
3. Prolactinomas
4. Infertility in women caused by hyperprolactinemia
5. Galactorrhea
6. Parkinson's disease.

21. Synthetic preparation of gonadotropin-releasing hormone (GnRH) is termed:
1. Nafarelin
2. Gonadorelin
3. Buserelin
4. Leuprorelin
5. Goserelin.

22. Peptides with gonadotropin-releasing hormone activity are which of the following?
1. Nafarelin
2. Menotropins
3. Buserelin
4. Goserelin
5. Gonadorelin

23. Which of the following GnRH analogues are more potent than the naturally occurring hormone?
1. Nafarelin
2. Menotropins
3. Buserelin
4. Goserelin
5. Gonadorelin

24. GnRH analogues can be administered by which of the following routes?
1. Sublingual
2. Subcutaneous
3. Intranasal
4. Rectal
5. Intramuscular

25. GnRH analogues administered in depot formulations are used:
1. to stimulate FSH and LG secretion.
2. to inhibit gonadotrophin release.
3. to treat infertility caused by hypogonadism.
4. to treat precocious puberty.
5. to treat prostate cancer and endometriosis.

26. Which of the following regimens of gonadorelin administration causes long-term stimulation of gonadotrophin secretion?
1. Continuous subcutaneous administration
2. Pulsatile subcutaneous administration

27. Continuous use of GnRH analogues results in all of the following, EXCEPT:
1. Transient stimulation of gonadotrophin release
2. Long-term stimulation of gonadotrophin secretion
3. Desensitisation of GnRH receptors in the pituitary
4. Long-term suppression of gonadotrophin secretion.

28. The urine of pregnant women has LH (luteinizing hormone)-like activity. A substance derived from the urine is which of the following?
1. Cosyntropin
2. Menotropines
3. Somatomedin
4. Follitropin
5. Human chorionic gonadotropin(hMG)

29. Which of the following are the main effects of human chorionic gonadotrophin?
1. Stimulation of testosterone production
2. Stimulation of spermatogenesis
3. Induction of ovulation

30. Which of the following drugs is a recombinant follicle-stimulating hormone (FSH)?
1. Cosyntropin
2. Menotropines
3. Bromocriptine
4. Follitropin
5. Human chorionic gonadotropin(hMG)

31. Drugs with FSH-like activity are which of the following?
1. Cosyntropin
2. Menotropines
3. Somatomedin
4. Follitropin
5. Human chorionic gonadotropin

32. Which of the following are main effects of human menopausal gonadotrophin (hMG, menotropines)?
1. Stimulation of testosterone production
2. Stimulation of spermatogenesis
3. Induction of mature follicle development

33. The main therapeutic uses of human menopausal and chorionic gonadotrophins are all of the following, EXCEPT:
1. Hypogonadism of pituitary or hypothalamic origin
2. In vitro fertilization programs
3. Female infertility caused by hyperprolactinemia
4. Anovulatory infertility caused by hypopituitarism.

34. Drugs which may be used in the treatment of infertility include which of the following?
1. Human chorionic gonadotrophin
2. Bromocriptine
3. Gonadotropin-releasing hormone (pulsatile administration)
4. Prolactin
5. Gonadotropin-releasing hormone (continuous administration)

35. Drugs which suppress release of gonadotrophins are all of the following, EXCEPT:
1. Danazol
2. Gonadotrophin-releasing hormone (pulsatile administration)
3. Gonadotrophin-releasing hormone (continuous administration).

36. Which of the following drugs is used to induce or reinforce labour?
1. Menotropins
2. Oxytocin
3. Vasopressin

37. When is the uterus more sensitive to oxytocin?
1. During the first trimester of pregnancy
2. During labour
3. In postpartum period
4. Before labour

38. Oxytocin causes all of the following effects EXCEPT:
1. Vasoconstriction
2. Regular coordinated contractions of the uterus
3. Contraction of myoepithelial cells in the mammary gland
4. Vasodilation
5. Weak antidiuretic action.

39. The pharmacological effects of vasopressin are all of the following, EXCEPT:
1. Antidiuretic effect
2. Relaxation of intestinal smooth muscles
3. Vasoconstriction
4. Promotion of ACTH release from the anterior pituitary
5. Release of coagulation factor VIII.

40. The action of vasopressin on smooth muscle tone is mediated by:
1. V_1- receptor
2. V_2-receptor
3. V_3-receptor.

41. Antidiuretic effect of vasopressin:
1. is mediated by V_3-receptors.
2. is mediated by V_2-receptors.
3. results from increased water permeability of cell luminal membranes in the collecting duct.
4. results from decreased insertion of water channels into the luminal membrane of collecting duct cells.

42. Which of the following drugs are used to treat pituitary diabetes insipidus?
1. Oxytocin
2. Lypressin
3. Somatotropin
4. Desmopressin
5. Bromocriptine

43. Which of the following statements concerning desmopressin compared with vasopressin are correct?
1. Its antidiuretic effect lasts longer.
2. It has a weaker selectivity for V_2-receptors.
3. Its selectivity for V_1-receptors is much higher.
4. It has less ability to cause vasoconstriction.
5. It has a more selective antidiuretic effect.

44. All of the following statements concerning therapeutic uses of desmopressin are correct EXCEPT:
1. Antidiuretic effect allows its use in the treatment of diabetes insipidus.
2. Its main use is in the treatment of bleeding oesophageal varices
3. It may be used for prophylaxis of bleeding in haemophilia A.
4. It is also indicated in persistent nocturnal enuresis.

45. Which of the following adverse effects are more common for vasopressin rather than for desmopressin?
1. Spasm of coronary vessels precipitating angina pectoris
2. Antidiuretic effect
3. Rise in blood pressure
4. Hyponatraemia

46. Which of the following vasopressin analogues are used due to their ability to cause vasoconstriction?
1. Oxytocin
2. Lypressin
3. Terlipressin
4. Desmopressin
5. Felypressin

47. Which of the following drugs are used for initial treatment of bleeding oesophageal varices?
1. Oxytocin
2. Lypressin
3. Terlipressin
4. Desmopressin
5. Vasopressin
6. Octreotide

48. Which of the following vasopressin analogues show much less antidiuretic activity than vasopressin itself?
1. Oxytocin
2. Lypressin
3. Terlipressin
4. Desmopressin
5. Felypressin

49. Which of the following vasopressin analogues show the same profile of activities as vasopressin?
1. Oxytocin
2. Lypressin
3. Terlipressin
4. Desmopressin
5. Felypressin

50. All of the following are hormones, EXCEPT:
1. Bromocriptine
2. Somatotropin
3. Thyrotropin
4. Prolactin
5. Sermorelin
6. Oxytocin.

51. All of the following statements are correct, EXCEPT:
1. Dopaminergic antagonists may cause hyperprolactinemia.
2. Bromocriptine restores ovulatory cycle in women with hyperprolactinemia.
3. Nasal oxytocin may be used for impaired milk ejection.
4. Nasal desmopressin is used in diabetes mellitus.

52. Actions of thyroxine include which of the following?
1. Stimulation of oxygen consumption
2. Acceleration of cardiac rate
3. Hypercholesterolemia
4. Increased appetite
5. Weight gain

53. Which of the following inhibit the thyroid hormone synthesis?
1. Iodine in small doses
2. Glyburide
3. Thiamazole
4. Propranolol
5. Propylthiouracil

54. Useful in the management of hypothyroidism are all of the following, EXCEPT:
1. Levothyroxine
2. Propylthiouracil
3. Liothyronine
4. Iodine in high doses.

55. Which of the following drugs is a preparation of triiodothyronine?
1. Levothyroxine
2. Propylthiouracil
3. Liothyronine
4. Thiamazol

56. Rapidly acting drug for the treatment of myxoedema coma is which of the following?
1. Levothyroxine
2. Propylthiouracil
3. High doses of iodine
4. Liothyronine
5. Calcitonin

57. Main adverse effects of thyroxine are which of the following?
1. Tachycardia
2. Tremor
3. Non-toxic goitre
4. Sweating
5. Nervousness
6. Drowsiness

58. The hazards of thyroxine overdose may be which of the following?
1. Risk of precipitating angina pectoris
2. Myxoedema coma
3. Cardiac dysrrhythmias
4. Increase of bone resorption leading to osteoporosis

59. Drugs used in the treatment of thyrotoxicosis include all of the following, EXCEPT:
1. Propylthiouracil
2. Iodine dissolved in potassium iodide (Lugol's solution)
3. Thyroglobulin
4. Radioactive iodine.

60. Which of the following drugs are useful in the treatment of thyrotoxicosis?
1. Propylthiouracil
2. Iodine (small amount)
3. Iodine in high dosage
4. Thiamazole
5. Propranolol

61. Which of the following is the symptomatic treatment used to control cardiac manifestations in thyrotoxicosis?
1. Propylthiouracil
2. Thiamazole
3. Triiodothyronine
4. Propranolol

62. Effects of iodine given in large doses include all of the following, EXCEPT:
1. Decrease of size of the hyperplasic thyroid gland
2. Long-lasting suppression of thyroid hormone synthesis
3. Decrease of thyroid hormone release in hyperthyroid individuals
4. Reduction in vascularity of the hyperplasic thyroid gland.

63. The main uses of iodine in large doses include:
1. long-term treatment of hypothyroid states.
2. short-term treatment before thyroid gland surgery.
3. thyrotoxic crisis.
4. iodine-induced thyrotoxicosis.

64. Treatment with thiamazole (methimazole) causes which of the following?
1. Decrease of the synthesis of thyroid hormones
2. Inhibition of the release of thyrotropin-releasing hormone
3. Agranulocytosis as an infrequent but the most dangerous adverse effec
4. Non-toxic goiter due to suppression of the negative feedback effect
5. Inhibition of thyroglobulin iodination

65. All of the following statements concerning propylthiouracil are correct, EXCEPT:
1. Mechanism of action is completely different from that of methimazol.
2. Like methimazol, it belongs to the chemical group of thioamides.
3. It is preferred in the treatment of thyroid storm.
4. It has an additional effect of reducing the conversion of T4 to T3.

66. Simple non-toxic goitre can be caused by:
1. long-term dietary iodine deficiency
2. antithyroid therapy with thioamides
3. treatment with thyroxine.

67. Which of the following agents tend to increase plasma concentration of calcium?
1. Calcitonin
2. Parathhormone
3. Vitamin D

68. Parathyroid hormone causes which of the following effects?
1. Mobilization of calcium from bone
2. Decrease of bone resorption
3. Stimulation the synthesis of calcitriol
4. Decrease of calcium absorption from the intestine
5. Increase of phosphate excretion
6. Increase in reabsorption of calcium by the kidney

69. Pharmacological effects of calcitonin are all of the following, EXCEPT:
1. Inhibition of bone resorption
2. Increase of osteoclast activity
3. Decrease of calcium reabsorption by the kidney
4. Increase of phosphate excretion.

70. Main therapeutic uses of calcitonin are which of the following?
1. Hypercalcaemia
2. Osteoporosis
3. Paget's disease (uncontrolled osteoclastic bone resorption)
4. Hypothyroidism

71. Which of the following agents inhibit bone resorption?
1. Calcitonin
2. Glucocorticoids
3. Estrogens
4. Bisphosphonates
5. Parathormone

72. Which of the following drugs are used in the treatment of osteoporosis?
1. Salcatonin
2. Prednisolone
3. Calcium salts + vitamin D
4. PTH in small doses given intermittently
5. Bisphosphonates
6. Raloxifene

73. All of the following statements concerning bisphosphonates are correct, EXCEPT:
1. Inhibition of bone resorption contributes to their therapeutic effect.
2. Decrease of osteoclast activity is their main effect.
3. Inhibition of bone mineralization contributes to their therapeutic effect.
4. They are pyrophosphate analogues, which are incorporated into the bone matrix.
5. Most common adverse effects of bisphosphonates are oesophagitis, peptic ulcer.

74. The main therapeutic uses of bisphosphonates are all of the following, EXCEPT:
1. Paget's disease
2. Hypercalcaemia caused by malignant disease
3. Hypocalcaemia
4. Osteoporosis

75. All of the following statements concerning vitamin D metabolites are correct, EXCEPT:
1. Vitamin D_3 (cholecalciferol) is converted to 25-hydroxyvitamin D3 (calcifediol) in the liver.
2. Calcitriol (1, 25-dihydroxyvitamin D_3) is formed in the kidney from calcifediol.
3. Calcitriol is inactive metabolite of vitamin D_3.
4. PTH regulates synthesis of calcitriol.
5. Calcitriol regulates its own production through negative feedback effect.

76. Which of the following metabolites of vitamin D3 are clinically available?
1. Calcifediol
2. Calcitriol
3. Salcatonin
4. Cholecalciferol
5. Alfacalcedol

77. Which of the following statements are true for calcitriol?
1. It regulates calcium and phosphate homeostasis.
2. It increases the reabsorption of calcium by the kidney.
3. It causes the decrease of phosphate excretion.
4. It inhibits osteoclast activity.
5. It is the most potent form of vitamin D3.

78. Which of the following are the mainstays of treatment of hypocalcaemia caused by hypoparathyroidism?
1. Calcitonin
2. Vitamin D
3. Bisphosphonates
4. Calcium salts
5. Parathormone

79. Which of the following drugs are used for the treatment of Type I diabetes?
1. Metformin
2. Nateglinide

3. Insulin
4. Tolbutamide
5. Pioglitazone

80. All of the following drugs are used for the treatment of Type II diabetes, EXCEPT:
1. Lispro ultra-rapid insulin
2. Metformin
3. Glipizide
4. Octreotide
5. Acarbose.

81. Insulin receptors are which of the following?
1. Membrane-bound receptors with tyrosine kinase activity
2. Membrane-bound receptors linked with sodium-channels
3. Intracellular receptor which regulate gene transcription
4. Membrane-bound G-protein-linked receptors

82. All of the following statements pertaining to the mechanisms of hypoglycemic action of insulin are correct, EXCEPT:
1. It stimulates glucose uptake by the cells.
2. It promotes glucose storage as glycogen.
3. It decreases absorption of starch and disaccharides.
4. It inhibits glycogenolysis.
5. It stimulates glycogenesis.

83. Effects of insulin include all of the following, EXCEPT:
1. Increase of protein synthesis in skeletal muscles
2. Increase of triglyceride synthesis in the adipose tissue
3. Increase of glycogenolysis in the liver cells
4. Inhibition of lipolysis in the adipose tissue
5. Inhibition of conversion of aminoacids and fatty acids to keto acids.

84. Correct statements about crystalline zinc (regular) insulin include all of the following, EXCEPT:
1. It is a short-acting insulin.
2. It can be administered intravenously.
3. It can be administered orally.
4. It is a good agent for the rapid control of diabetic ketoacidosis.

85. The longest-acting insulin preparation is which of the following?
1. Human NPH (isophane) insulin
2. Regular (crystalline zinc) insulin
3. Ultralente insulin
4. Lente insulin

86. Which of the following drugs have the common mechanism of action in the treatment of diabetes?
1. Tolbutamide
2. Pioglitazone
3. Repaglinide
4. Glipizide
5. Metformin

87. Sulfonylureas are which of the following?
1. Tolbutamide
2. Pioglitazone
3. Repaglinide
4. Glipizide
5. Metformin

88. The main mechanism of hypoglycemic action of sulfonylureas is which of the following?
1. Stimulation of insulin release from the pancreas
2. Inhibition of gluconeogenesis
3. Reduction of serum glucagon level
4. Inhibition of α-glucosidase
5. Increase of insulin binding to its receptors

89. Which of the following statements concerning the mechanism of sulfonylureas action are correct?
1. They block ATP-sensitive potassium channels causing depolarization of the membrane of pancreatic β cells.
2. They cause depolarization of the membrane of pancreatic β cells due to increased sodium influx.
3. Insulinotropic effect of sulfonylureas resembles that of glucose.
4. Sulfonylureas increase conversion of glucose to lactate by enterocytes.
5. Increased influx of Ca^{2+} results in stimulation of insulin release from the pancreas.

90. All of the following statements concerning the action of sulfonylureas are correct, EXCEPT:
1. They do not stimulate insulin synthesis.
2. Glipizide is a longer acting drug than glybenclamide.
3. Hypoglycemia is likely to be a serious complication of sulfonylurea therapy.
4. Less response to sulfonylurea therapy in obese diabetics is possibly due to insulin resistance.

91. Which of the following drugs belong to second-generation sulfonylureas?
1. Tolbutamide
2. Glipizide
3. Chlorpropamide
4. Glybenclamide
5. Nateglinide
6. Glimepiride

92. Which of the following statements concerning meglitinides are correct?
1. They block ATP-sensitive potassium channels of the pancreatic β- cells and cause the release of insulin.
2. Nateglinide has a very fast onset and short duration of action.
3. Given before meal they decrease postprandial level of insulin.
4. They are used before each meal to decrease postprandial level of glucose.

93. All of the following statements concerning metformin are correct, EXCEPT:
1. Metformin rather than sulfonylureas is preferred in patients with resistance to insulin.
2. Reduction in hepatic gluconeogenesis contributes to the mechanism of antidiabetic action.
3. Increase of insulin release is its main effect in the treatment of diabetes.
4. It causes normalization of blood glucose level rather than hypoglycemia.
5. It is associated with the risk of lactic acidosis.

94. Drugs which reduce insulin resistance of target tissues are which of the following?
1. Tolbutamide
2. Pioglitazone
3. Chlorpropamide
4. Glipizide
5. Metformin

95. Which of the following statements concerning thiazolidinediones are correct?
1. They diminish insulin resistance and increase the action of endogenous insulin.
2. Synthesis and translocation of glucose transporter GLUT4 contributes to increased glucose uptake in the target tissue.
3. Inhibition of α-glucosidase is the additional mechanism of their action.
4. The beneficial effect of these drugs is a decline in visceral fat mass.
5. Hypoglycemia is likely to be the common complication of the therapy.

96. Which of the following drugs are α-glucosidase inhibitors?
1. Miglitol
2. Acarbose
3. Pioglitazone
4. Glipizide
5. Metformin

97. All of the following statements concerning α-glucosidase inhibitors are correct, EXCEPT:
1. They reduce postprandial digestion and absorption of starch and disaccharides.
2. Acarbose is mainly used in patients with Type I diabetes.
3. Unlike acarbose, miglitol is systemically absorbed.
4. The appearance of undigested carbohydrate in the colon causes flatulence, diarrhea, abdominal cramping.
5. α-Glucosidase inhibitors are used as monotherapy in Type II diabetes.

98. Which of the following drugs do not appear to cause hypoglycemia when they are used as monotherapy?
1. Acarbose
2. Glipizide
3. Repaglinide
4. Metformin
5. Pioglitazone

99. Oral hypoglycemic agent that is associated with increased incidence of lactic acidosis is which of the following?
1. Ultralente insulin
2. Glyburide
3. Metformin
4. Nateglinide

4. TASKS

TASK 1

The table describes the effects of insulin on carbohydrate, fat and protein metabolism in the liver, muscle and adipose tissue. Show the character of metabolic effects of insulin by putting the appropriate arrows (↑ - increase, ↓ - decrease) into each cell.

	Liver cells		Fat cells		Muscle cells	
Carbohydrate metabolism	Gluconeogenesis Glycogenolysis Glycolisis Glycogenesis		Glucose uptake		Glucose uptake Glycogenesis Glycolisis	
Fat metabolism	Lipogenesis Lipolisis		Synthesis of tryglycerides and fatty acids Lipolisis			
Protein metabolism	Protein breakdown				Amino acid uptake Protein synthesis	

TASK 2

The table illustrates the main effects of antidiabetic drugs underlying their hypoglycemic action. Based on the effects on carbohydrate metabolism shown in the table put the names of the drugs: *Glibenclamide, Pioglitazone, Acarbose, Insulin, Metformin, Nateglinide* into the appropriate cells

Drugs / Metabolic parameters						
Gluconeogenesis	↓	↓				
Glucose uptake	↑	↑		↑		
Glycogenolysis		↓				
Insulin secretion			↑			↑
Intestinal absorption of glucose	↓				↓	
Insulin sensitivity of target tissue	↑			↑		

TASK 3

Study the table describing the main adverse effects of antidiabetic drugs. Put the name of each of the following drugs: *Metformin, Glibenclamide, Pioglitazone, Acarbose* into the appropriate cell according to their adverse effects.

Drugs / Adverse effects				
Hypoglycemia	+			
Increase of appetite	+			
Anorexia	-		+	
Weight gain	+			+
Weight loss	-		+	
Lactic acidosis			+	
Oedema				+
Flatulence and abdominal pain		+		

Note: Increased insulin secretion leads to hypoglycemia which can be severe and prolonged. Hypoglycemia is associated with increased appetite and weight gain. These effects belong to undesirable effects and appear to be the main drawback of the therapy with sulfonylureas. Oppositely, decrease of appetite and weight loss caused by biguanides are considered to be very useful in the obese patients with type II diabetes (NIDDM)

TASK 4

The table describes the effects of hormones regulating calcium and phosphate turnover. Put the appropriate arrow (↑ - increase, ↓ - decrease) into each cell based on the character of these effects.

Drugs / Parameters	Calcitonin	Parathormon	Calcitriol
Intestinal calcium absorption			
Renal calcium excretion			
Renal phosphate excretion			
Mobilization of calcium from bone			
Calcium serum concentration			
Osteoclast activity			

TASK 5

The table describes the uses of hormone analogues in diagnosis of certain endocrine dysfunctions. Specify the uses of each preparation ticking the appropriate cell.

Preparations / Dignostic test	Sermorelin	CRF	Tetracosactide	Protirelin
Adrenal cortical insufficiency			+	
GH secretion insufficiency	+			
Pituitary or hypothalamic defect in ACTH deficiency		+		
Thyroid dysfunctions				+

TASK 6

Identify each of the following drugs: based on their main therapeutic uses shown in the table.

Drugs / Therapeutic uses						
Diabetes insipidus	+					
NIDDM			+			
Bleeding oesophageal varices	+	+				
Galactorrhea				+		
Acromegaly		+		+		
Endometriosis						+
Pituitary adenomas		+				
Anovulatory infertility					+	
Hypogonadotropic hypogonadism in males					+	
Prostate cancer						+
Parkinson's disease				+		

TASK 7

Answer the following questions in the spaces provided.

7.1. Explain the concept of negative feedback in the control of hormone secretion.

7.2. What physiological effects are produced by the thyroid hormones T_3 and T_4 and what is the mechanism of their action at molecular level? What are the main differences between these hormones? Specify the difference between their uses.

7.3. What is the rationale for the treatment of hypothyroidism? Explain why TSH level is an accurate marker of thyroid hormone activity in the blood.

7.4. What drugs are available for treating hyperthyroidism? Specify their mechanisms of action and clinical applications (long-term therapy or short-term thyroid suppression).

7.5. How does the action of the antithyroid drugs differ from the action of radioactive iodide? What is the difference in their uses?

7.6. What pathological condition is associated with goiter? Explain it. What antithyroid drugs are referred to as goitrogens? Specify the mechanism of goitrogenic action of these drugs.

7.7. What is the difference between pulsatile and continuous use of GnRH (gonadorelin) and its analogues (specify the mechanism of action, regulation of gonadotrophin release and clinical uses)?

7.8. Specify the difference between hCG and hMG. What do they have in common and what are their main clinical uses?

7.9. Name the common clinical application of octreotide and bromocriptin and specify the effect that underlies it. Do these drugs belong to the same pharmacological group? Name their other effects and clinical uses.

7.10. Specify the difference between vasopressin, desmopressin and terlipressin. What are their main clinical uses and the effects that underlie each of them?

7.11. What hormones control calcium metabolism? How do these hormones differ?

7.12. Specify hormones which decrease (1) and increase (2) bone resorption. Which of them can be used in the treatment of osteoporosis?

1.

2.

7.13. Specify the effects of calcitonin and its main clinical uses.

7.14. Describe the mechanism of action of bisphosphonates, their main effects and therapeutic uses.

7.15. What is the difference between Type I and Type II diabetes? What drugs are recommended for the control of each of these types of diabetes?

7.16. What are common symptoms of diabetes? How does insulin control the symptoms of diabetes?

7.17. Specify metabolic effects of insulin which contribute to the decrease of blood glucose level? What molecular mechanism underlies these effects?

1.

2.

3.

4.

7.18. How do the commercial insulin preparations differ? Preparations of which origin are considered to be the best?

7.19. Which insulin preparations are used for acute hyperglycemia (1) and which are recommended to provide basal insulin level through the night (2)? What is the main difference between these preparations?

1.

2.

7.20. What is the main danger of insulin therapy? What should be done if complications of excessive insulin develop?

7.21. Which hypoglycemic drugs increase insulin secretion? Specify the mechanism of this action.

7.22. What should be done to control postprandial glucose level and what drugs should be used?

1.

2.

7.23. Which undesirable effects in patients with diabetes are caused by the hypoglycemic action of insulin and sulfonylureas? In which patients are sulfonylureas not recommended?

7.24. Name oral antidiabetic drugs which belong to insulin sensitizers. What is the advantage of these drugs?

7.25. Which drugs are recommended for the treatment of Type II diabetes in obese patients? Explain their benefits in this case.

7.26. Specify the mechanisms of action of biguanides in diabetes mellitus.

1.

2.

3.

4.

7.27. What is the most serious adverse effect which may occur in patients taking metformin? Specify conditions which predispose to this adverse effect.

TASK 8

For each numbered item, select the ONE lettered option that is most closely associated with it. Each lettered option may be selected once, more than once, or not at all.

A. Octreotide
B. Metformin
C. Leuprolide
D. Thimazole
E. Triiodothyronine
F. Thyrotropin
G. Glibenclamide
H. Lugol's solution
I. Repaglinide

8.1. The active hormone produced in the peripheral tissues when thyroxine is administered.

8.2. Somatostatin analogue used in the treatment of acromegaly and pituitary adenomas.

8.3. The drug recommended for the treatment of Type 2 diabetes in obese patients.

8.4. The drug used for long-term therapy of hyperthyroidism.

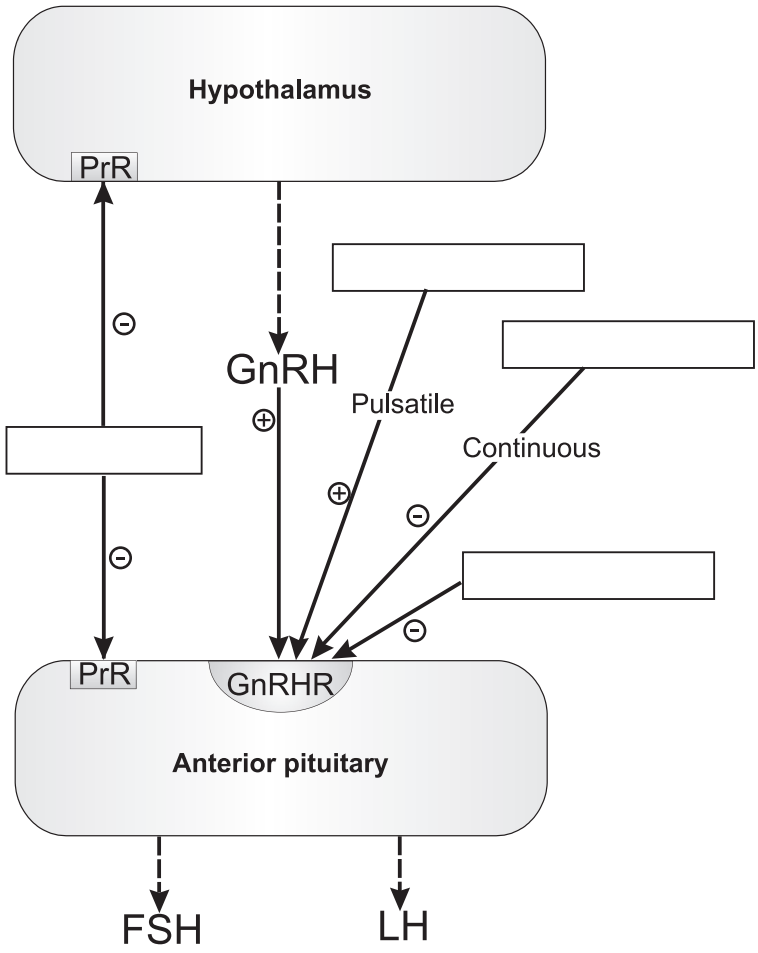
8.5. The analogue of GnRH which is administered continuously to suppress gonadotrophin release.

8.6. The drug recommended for use in controlling postprandial glucose level in Type II diabetes.

8.7. This drug contains iodine in high dosage and exerts a transient thyrostatic effect in thyrotoxic crisis.

TASK 9

Study the diagram illustrating the control of LH and FSH release and identify the localization of action of the following drugs: *gonadorelin, leuprolide, danazol, cetrorelix.* Fill in the boxes with the names of the appropriate drugs.

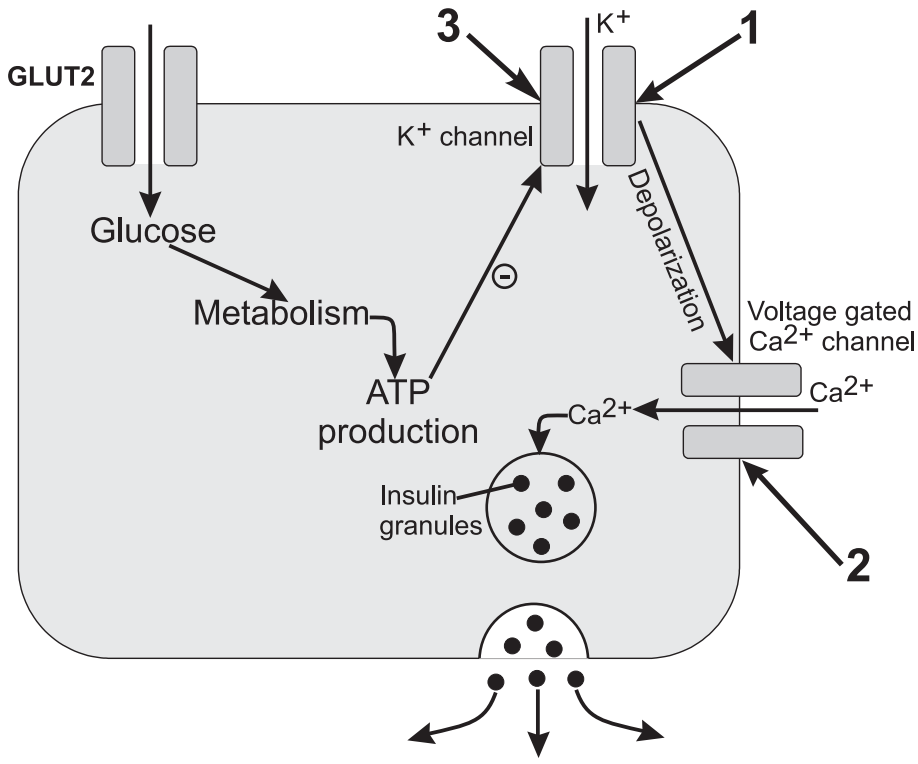


GnRH - gonadotrophin-releasing hormone
GnRHR - gonadotrophin-releasing hormone receptor
PrR - progesterone receptor
FSH - folicle-stimulating hormone
LH - luteinizing hormone

Explain the mechanisms of action of *gnadorelin, leuprolide and cetrorelix* and specify their clinical uses in the spaces provided

TASK 10

The mechanism of action of which of the following drugs: *acarbose, glibenclamide, metformin, repaglinide, pioglitazone* does this diagram illustrate? Identify the localization (1,2,3) and character (+ or -) of action of the selected drugs.



Specify the mechanism of hypoglycaemic action of drugs given in the table below.

Acarbose	Glibenclamide	Metformin	Repaglinide	Pioglitazone

5. CASES

CASE 1

A 23-year-old woman with IDDM wishes to try close control of her postprandial glucose level and to improve her long-term prognosis. Which of the following regimens is the most appropriate?

1. Morning injections of mixed lente and ultralente insulins
2. Evening injections of mixed regular and lente insulins
3. Morning and evening injections of regular insulin, supplemented by small amounts of ultralente insulin at mealtimes

4. Morning injections of ultralente insulin, supplemented by small amounts of insulin Lispro at mealtimes
5. Morning injection of semilente insulin and evening injection of lente insulin.

Explain your choice in the space provided.

CASE 2

A 13-year-old boy with Type I diabetes (IDDM) is brought to hospital complaining of dizziness. Laboratory findings include severe hyperglycemia, ketoacidosis, and the blood pH of 7,15.

a) In order to achieve rapid control of the severe ketoacidosis in this diabetic boy, the appropriate antidiabetic agent to use is:
   1. Regular (Crystalline zinc insulin)
   2. Lente insulin
   3. Isophane (NPH) insulin
   4. Tolbutamide
   5. Ultralente insulin

b) The most likely complication of insulin therapy in this patient is:
   1. Dilutional hyponatremia
   2. Hypoglycemia
   3. Increased bleeding tendency
   4. Pancreatitis
   5. Severe hypertension

Explain selection of the treatment. What should be made in the case of severe complication of insulin therapy?

CASE 3

A poorly controlled patient with NIDDM receiving oral hypoglycemic therapy is complaining of hunger, sweating, and palpitations. Examination reveals moist, pale skin and hypothermia.

1) Which one of the following can be deduced from the patient's symptoms?
   1. The symptoms are caused by hyperglycemia.
   2. The dose of a hypoglycemic drug is probably too low.
   3. The symptoms are premonitory of hypoglycemic shock.

2) Which group of drugs is this patient most likely to receive?
   1. α-Glucosidase inhibitors
   2. Sulfonylureas
   3. Thiazolidindiones
   4. Biguanides

3) Which of the following drugs should be recommended for the treatment in order to avoid such complications?
   1. Ultralente insulin
   2. Glimepiride
   3. Metformin
   4. Repaglinide

Explain your choice.

CASE 4

A 44-year-old moderately obese woman is diagnosed with Type II diabetes mellitus (NIDDM). Dietary modifications and sulfonylurea therapy fail to control the patient's glucose levels. Which oral antidiabetic agent with a minimal risk of causing hypoglycemia and weight gain should be prescribed for this patient?
1. Repaglinide
2. Glipizide
3. Glyburide
4. Metformin
5. Tolbutamide

Explain your choice.

CASE 5

A 43-year-old woman with the history of renal failure is diagnosed with Type II diabetes mellitus. Dietary modifications fail to control the patient's glucose levels. Therapy associated with hypoglycemia should be avoided because renal failure makes diabetic patients very vulnerable to hypoglycemia. Which oral antidiabetic agent with a minimal risk of causing hypoglycemia should be prescribed?
1. Nateglinide
2. Metformin
3. Pioglitazone

4. Glipizide
5. Glibenclamide

Explain your choice.

CASE 6

A 43-year-old obese patient with Type II diabetes and a history of alcoholism should probably not receive metformin because it can increase his risk of:

1) 1. A disulfiram-like reaction
   2. Excessive weight gain
   3. Hypoglycemia
   4. Lactic acidosis
   5. Serious hepatotoxicity
2) Which of the following drugs can be recommended for the treatment aiming to prevent weight gain?
   1. Insulin
   2. Acarbose
   3. Pioglitazone
   4. Glipizide
   5. Glibenclamide

Explain your choice.

CASE 7

A 37-year-old woman complains to her family physician of weight gain, constipation and lethargy. On examination moderate bradycardia, mild hypertension, slowing of speech have been found. The results of the laboratory test (low serum level of thyroxine, high serum TSH) along with the previous findings allow the diagnosis of primary hypothyroidism (thyroid gland dysfunction) to be made. The most common cause of this condition is autoimmune (Hashimoto's) thyroiditis. Explain the mechanism of rise in TSH level in this condition.

Choose the most appropriate treatment for the patient aiming to normalize the serum TSH level.
1. Long-term treatment with levothyroxine
2. Propylthiouracil plus iodide in large doses
3. Long-term treatment with liothyronine
4. Long-term treatment with thiamazol
5. Short-term treatment with amiodarone

CASE 8

A 45-year-old woman experienced nervousness, muscle weakness, tremor and premature beats. She suffered from insomnia and complained of weight loss despite the increased appetite. After severe angina attack she was brought to hospital. Laboratory tests showed high serum level of thyroid hormones and low level of TSH. On examination exophthalmos and enlargement of the thyroid gland confirmed the previous diagnosis of Graves' disease, the most common type of hyperthyroidism.

What is the most appropriate long-term treatment of this condition aiming to decrease the level of thyroid hormones?
1. Propylthiouracil
2. Iodine (small amount)
3. Iodine in high dosage
4. Thiamazole
5. Propranolol

Explain the drug choice and specify the action of the drug.

What therapy should be considered in the case of thyrotoxic crisis (thyroid storm)?

CASE 9

A 58-year-old postmenopausal woman with a small bone fracture is diagnosed with osteoporosis. The patient does not want to take estrogen therapy but is willing to take calcium and vitamin D supplements. Which other drugs could the physician prescribe to stop the progression of osteoporosis?
1. Alendronate
2. Finasteride
3. Hydrochlorothiazide
4. Leuprolide
5. Salcatonin

Explain the drug selection and specify the action of selected drugs. What treatment is preferred?

CASE 10

A 30-year-old woman with endometriosis has visited a clinic for appropriate treatment to be prescribed. Which drugs and regimens of administration of the given below can be recommended?

1. Leuprolide as parenteral depot suspension
2. Gonadorelin for intravenous pulsatile administration
3. Sermorelin for s/c injection
4. Nafarelin as nasal spray
5. Danazol as oral capsules

Explain the mechanism of selected treatment in endometriosis.

CASE 11

A 53-year-old man suffers from water diarrhea, hypokalemia, renal failure, and a VIPoma that arose in the pancreas and metastasized to other sites. After the pancreatic tumor is removed, which of the following drugs is most likely to be given to inhibit the release of vasoactive intestinal polypeptide (VIP) from the sites of metastases?

1. Leuprolide
2. Nafarelin
3. Octreotide
4. Protirelin
5. Sermorelin

Explain the drug selection and specify the action of selected drugs in this case.

CASE 12

A 27-year-old woman with amenorrhea, infertility, and galactorrhea was treated with a drug that successfully restored ovulation and menstruation. Before being given the drug, the woman was carefully questioned about previous mental health problems, which she did not have. She was advised to take the drug orally. The drug used to treat this patient was probably which of the following:

1. Bromocriptine
2. Desmopressin
3. Human chorionic gonadotropin
4. Gonadorelin (pulsatile)
5. Octreotide

Explain the drug choice and specify the action of the drug. Why should this drug not be used in patients with psychotic illness?

CASE 13

A 47-year-old man exhibited signs and symptoms of acromegaly. Radiologic studies showed the presence of a large pituitary tumor. Surgical treatment of the tumor was only partially effective in controlling his disease. At this point, which of the following drugs is most likely to be used as pharmacologic therapy?

1. Cosyntropin
2. Desmopressin
3. Leuprolide
4. Octreotide
5. Somatropin

Explain the drug choice and specify the action of the drug. What are other possible therapeutic uses of this drug?

CASE 14

A 25-year-old man develops excessive thirst after sustaining a severe head injury with a fracture at the base of the skull. His daily water intake is 5-6 L, and because of the ensuing polyuria, he has to get up several times during the night to void. The patient's clinical and laboratory findings are consistent with the diagnosis of diabetes insipidus due to damage of the hypothalamus that occurs rather frequently after head trauma. Which of the following is the treatment of choice for this patient?

1. Administration of anterior pituitary gland extract

2. Administration of vasopressin
3. Reduction of water intake
4. Administration of desmopressin
5. Administration of terlipressin

Explain the selection of the treatment and its advantage.