

PHARMACOLOGY – Endocrine drugs

1. A 30 year old woman commenced treatment for thyrotoxicosis last month. She presents with fevers and mouth ulcers. Her neutrophil count is $0.3 \times 10^9/L$. The most likely drug culprit is
 - A. carbimazole ✓
 - B. prednisolone
 - C. propranolol
 - D. radioactive iodine
2. Thyroxine is
 - A. best absorbed in the jejunum
 - B. more bioavailable in the T4 form
 - C. poorly absorbed in severe myxoedema ✓
 - D. potentially toxic in severe renal failure
3. All of the following affect the metabolism of thyroxine except for
 - A. carbamazepine
 - B. HIV protease inhibitors
 - C. oral contraceptives ✓
 - D. rifampicin
4. The action of thyroxine depends on
 - A. cAMP dependent activation of the Na K ATPase
 - B. increased DNA synthesis
 - C. increased RNA synthesis ✓
 - D. reduced 5'-deiodinase activity
5. Dexamethasone has
 - A. less potent anti-inflammatory action than methylprednisolone
 - B. longer duration of action than prednisolone ✓
 - C. nearly identical structure to cortisol
 - D. significant salt-retaining action
6. The geriatricians suggest starting a syncopal gentleman on fludrocortisone. You question this because he also has
 - A. hypercalcaemia
 - B. hyperglycaemia ✓
 - C. hyperkalaemia
 - D. hyponatraemia
7. Sitagliptin
 - A. causes more hypoglycaemia than sulfonylureas
 - B. has active metabolites
 - C. inhibits SGLT-2
 - D. is excreted in the urine ✓
8. Sulfonylureas act via
 - A. decreasing intestinal glucose absorption
 - B. receptors in the liver, muscle and adipose tissue
 - C. release of preformed insulin from the pancreas ✓
 - D. unclear mechanisms

9. NPH insulin has a duration of action of
- A. 3-5 hours
 - B. 4-12 hours ✓
 - C. 8-16 hours
 - D. 12-24 hours
10. Glucagon has the following effect:
- A. increases cardiac output ✓
 - B. reduces heart rate
 - C. relaxes vascular smooth muscle
 - D. stimulates intestinal smooth muscle
11. Metformin
- A. is extensively plasma protein bound
 - B. metabolises to active forms in the liver
 - C. provokes hypoglycaemia in the fasting state
 - D. reduces hepatic gluconeogenesis ✓
12. Mr Large has type 2 diabetes and reports intolerance to metformin treatment. The most common treatment-limiting side effect of metformin is
- A. allergic dermatitis
 - B. B12 deficiency
 - C. persistent diarrhoea ✓
 - D. renal impairment

1. What is the mechanism of action of carbimazole?

Carbimazole is converted to methimazole in vivo and, along with propylthiouracil, they are all thioamines.

Methimazole is ten times as potent as propylthiouracil. Propylthiouracil has a black box warning for severe hepatitis so is reserved for 1st trimester of pregnancy as it doesn't cross the placenta as readily, in thyroid storm and those with a reaction to methimazole.

Thioamides act by multiple mechanisms. The major action is to prevent hormone synthesis by inhibiting the thyroid peroxidase-catalyzed reactions and blocking iodine organification. In addition, they block coupling of the iodotyrosines. They do not block uptake of iodide by the gland. Propylthiouracil but not methimazole also inhibits the peripheral deiodination of T₄ and T₃ (Figure 38–1). Since the synthesis rather than the release of hormones is affected, the onset of these agents is slow, often requiring 3–4 weeks before stores of T₄ are depleted.

2. What are the pharmacological effects of glucagon?

A. Metabolic Effects

The first six amino acids at the amino terminal of the glucagon molecule bind to specific G_s protein-coupled receptors on liver cells. This leads to an increase in cAMP, which facilitates catabolism of stored glycogen and increases gluconeogenesis and ketogenesis. The immediate pharmacological result of glucagon infusion is to raise blood glucose at the expense of stored hepatic glycogen. There is no effect on skeletal muscle glycogen, presumably because of the lack of glucagon receptors on skeletal muscle. Pharmacological amounts of glucagon cause release of [insulin](#) from normal pancreatic beta cells, catecholamines from pheochromocytoma, and calcitonin from medullary carcinoma cells.

B. Cardiac Effects

Glucagon has a potent inotropic and chronotropic effect on the heart, mediated by the cAMP mechanism described above. Thus, it produces an effect very similar to that of β -adrenoceptor agonists without requiring functioning β receptors.

C. Effects on Smooth Muscle

Large doses of glucagon produce profound relaxation of the intestine. In contrast to the above effects of the peptide, this action on the intestine may be due to mechanisms other than adenylyl cyclase activation.