GH(Somatotropin) & Somatostatin

Recombinant human growth hormone (rhGH): Uses: Replacement therapy in growth hormone deficient patients. It is also used to promote growth for patients with Turner syndrome (link to genetics).

Mecasermin- rhIGF-1
mecasermin rinfabate- complex of rhIGF-1 and its binding protein (rhIGFBP-3)

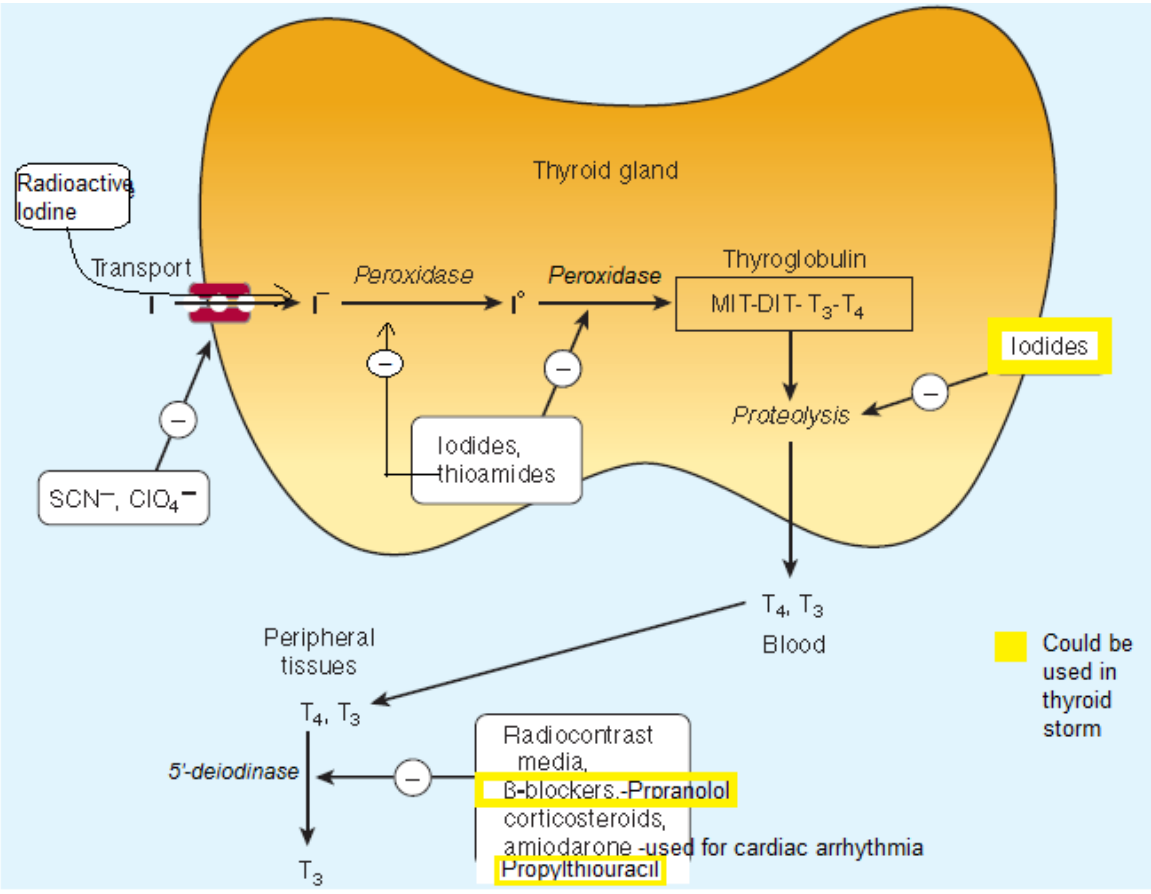
<u>GH antagonists:</u>

1. **Octreotide** (Somatostatin analog): Uses:
   hormone-secreting tumors;
   gastrinoma, glucagonoma, VIPoma,
   Acromegaly
   Carcinoid syndrome
   Bleeding from esophageal varices.

2. **Bromocriptine** (Dopamine receptor agonist)

3. **Pegvisomant** (GH receptor antagonist)- A Polyethylene glycol. Normalize IGF-1 levels, does not inhibit GH secretion.

Thyroid & Antithyroids



Antithyroids:

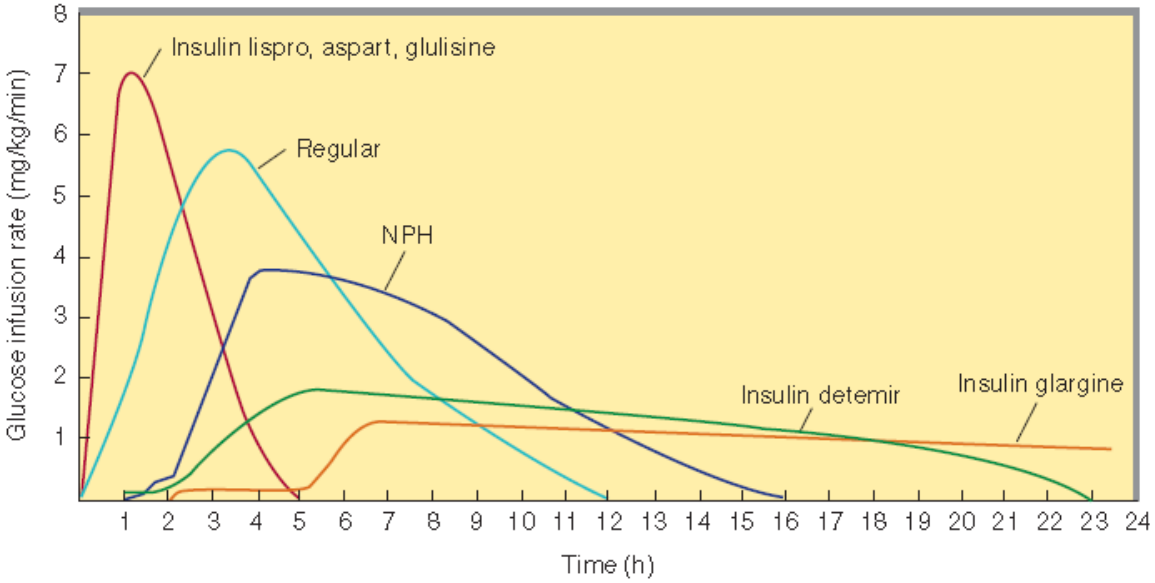
1. Thionamides- **Methimazole** and Propylthiouracil:
   Slow effect.
   Adverse effects: (1)Maculopapular rash-common (2)hepatitis-more severe and fatal with PTU (3)Agranulocytosis- potentially fatal. G-CSF speed recovery. (4) Cholestatic jaundice- more common with methimazole
   PTU for
   - *P*regnancy (cross the placenta less readily than methimazole because it is highly protein bound (they both cross the placenta)) ,
   - in thyroid storm (because it blocks *P*eripheral *conversion* of T4 into T3),
   - Back up for methimazole (in case of adverse reactions).
2. **Iodides**
   Reduce Vascularity, size, fragility of the thyroid gland -> used preoperatively.
   Not to be used alone-> the gland "escapes" from iodine block in 2-8 weeks.
3. β-adrenergic blockers (propranolol)
   Do not typically alter thyroid hormone levels but used in they control tachycardia associated with hyperthyroidism in addition to inhibition of peripheral conversion of T4 to T3.
   Patients with bronchial asthma: Diltiazem is an alternative.

Levothyroxine & Liothyronine
Replacement therapy for T4 and T3 respectively.
Levothyroxine is the first choice for replacement of thyroid hormones.

Antidiabetics

Insulin secretion: stimulated by: glucose, β-adrenergic activity, sulfonylureas.
Inhibited by: α-adrenergic activity.

Imsulin preparations	**MOA**	Bind to insulin receptor (tyrosine kinas). Increase glucose uptake and glycogen formation. Stimulate amino acids uptake and protein synthesis in skeletal muscle. Increase storage of triglycerides in adipose tissue.		
	Complications	Hypoglycemia-most common. Insulin allergy, immune insulin resistance (IgG ant insulin abs)		
	Onset	**Peak**	**Duration**	**Use**
Rapid acting lispro, Aspart, Glulisine	Fast onset, (5-15 mins)	1 hour	Short duration (<4-5 hours). Less risk of postmeal hypoglycemia	Postprandial glucose control
Short acting Regular insulin	Rapid onset (30 min)	2-3 hours	5-8 hours	IV for diabetic ketoacidosis
Intermediate acting. NPH	2-5 hours		4-12 hours	
Long acting Glargine, Detemir	1-1.5 hours	peakless	>11-24 hours	Background insulin replacement



	Oral antidiabetics	MOA	Use	Complications
Hypoglycemics	Sulfonylurea **1st generation: Tolbutamide, Chlorpropamide** **2nd generation: Glyburide, Glipzide, Glimepride**	Stimulate insulin secretion through inhibiting the efflux of K+ to beta cells of the pancreas	Type 2 DM.	Hypoglycemic reactions (less in glipizide), Weight gain, Disulfiram-like reaction with 1st generation drugs. DO NOT use in patients with renal impairment
	Meglitinides **Rapeglinide**	Like Sulfonylureas Fast onset, peak effect at 1 hour.	Type 2 DM, taken before meals to control postprandial hyperglycemia.	Can be used in patients with renal impairment and the elderly.
Euglycemics	**Biguanides** Metformin	DOES NOT depend on functioning pancreatic beta cells. Activate AMPK, reduce gluconeogenesis, slows absorption from GIT and stimulates glycolysis.	First line therapy for type 2 DM	GI disturbances, Lactic acidosis. Contraindicated in patients with renal or cardiac diseases. DOES NOT increase body weight or provoke hypoglycemia.
	Thiazolidinediones	Ligand to PPAR-γ. This receptor modulates the	Only to patients who remain	Fluid retention (contraindicated to

	Pioglitazone, Rosiglitazone	expression of genes involved in lipid and glucose metabolism and insulin signal transduction. GLUT-4 and adiponectin increase, FA levels and hepatic glucose output decrease. Thus increasing insulin sensitivity.	hyperglycemic despite use of other antidiabetics. As monotherapy or in combination for type 2 DM	patients with heart failure), macular edema, weight gain, bone fractures, hepatotoxic.
Amylin Analogues Pramlintide		Slow gastric emptying, reduce glucagon, reduce appetite.	Subcutaneous, for type 1 and type 2 DM	Hypoglycemia; concurrent mealtime insulin should be decreased. Nausea
GLP-1 affecting drugs	Exantide GLP-1 analogue	Glucagon like peptide-1 (GLP-1) enhances insulin release.	subcutaneous	Nausea, vomiting, pancreatitis, NO hypoglycemia unless used in combination- oral hypoglycemic dosage need to be decreased
	Stigaliptin	Inhibit DPP-4. DPP-4 degrades GLP-1	Type 2 DM, orally	Nasopharyngitis, URT infections.
α-glucosidase inhibitors Acarbose, Miglitol		Inhibits enteric α-glucosidase attached to the brush border of intestinal cells. Reduce postprandial hyperglycemia, delay absorption of sugars. Spares insulin.	Type 2 DM	Flatulence, diarrhea. Hypoglycemia if used with combination- treat with glucose NOT sucrose. Use in caution in hepatic disease.
SGLT-2 inhibitors Canagliflozine		Block resorption of glucose in the proximal tubules, increase urinary glucose loss		Genital and urinary tract infections. Hypotension. Contraindicated in renal dysfunction.

You can notice that these drugs either target insulin (risk of hypoglycemia) or target glucose itself (No risk of hypoglycemia unless used with combinations)

To use oral antidiabetics, check liver functions. Metformin and Canagliflozine need intact kidneys too.

Agents that affect bone and mineral homeostasis.

Teriparatide- Recombinant DNA parathyroid hormone analog 1-34, stimulate newbone formation and osteoblastic activity.

Vitamine D analogs- they all have "Calci" in their name:

- **Calcipotrien** for psoriasis
- **Doxercalciferol** and **paricalcitol**: for hyperparathyroidism secondary to chronic kidney disease.
- **Eldecalcitol**: for osteoporosis. "Osteoporosis is more common in elderly"

Raloxifene. Selective estrogen receptor modulator. It is an agonist on bone and antagonist on breast (No breast cancer risk) Protect against spine fractures but not hip fractures.

Bisphosphonates "Dronates"-

Pyrophosphate analogs. Stabilize hydroxyapatite. Inhibit mature osteoclast-mediated bone resorption through induction of osteoblasts to secrete osteoclast inhibitors (While other agents inhibit maturation of osteoclasts not the action of mature osteoclasts themselves).

Adverse effects:
1. Gastric and esophageal irritation (alendronate). Patients should take the drug with a large cup of water and remain in the upright position for 30 min.
2. Mineralization defects (etidronate and pamidronate)

Clinical uses:
1. Hypercalcemia of malignancy
2. Paget's disease
3. Osteoporosis- both postmenopausal and glucocorticoid induced.

Denosumab- monoclonal antibody for RANKL
Adverse effects:
1. Infections
2. Transiet hypocalcemia

Calcimimetics (**Cinacalcet**)
Activate CaSR in the parathyroid gland, blocks PTH secretion
Used for primary (parathyroid carcinoma) and secondary (chronic kidney disease) hyperparathyroidism.

Thiazide diuretics
Enhance calcium resorption in the distal tubules.
Used for hypercalciurea and calcium oxalate stones.

Strontium ranelate- increase bone formation, decrease bone resorption.