GROWTH HORMONE ANTAGONISTS

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Pharmacology Dept

Endocrine module

Objectives

- Enlist GH antagonists
- Describe clinical role of Octreotide in acromegaly
- Describe the
  - route of administration
  - dosage
  - adverse effects of Octreotide

  in acromegaly and gigantism
- Describe the mechanism of action, clinical uses, and adverse effects of Bromocriptine

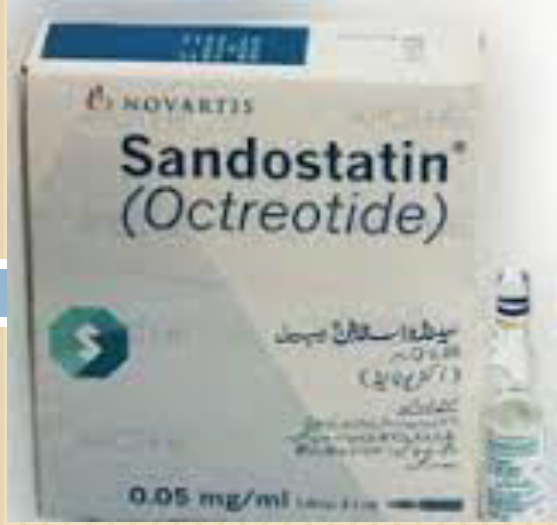
GH antagonists

- Somatostatin analogs
  - Octreotide
  - lanreotide
- Dopamine receptor agonists
  - Bromocriptine
  - cabergoline
- GH receptor antagonist
  - pegvisomant

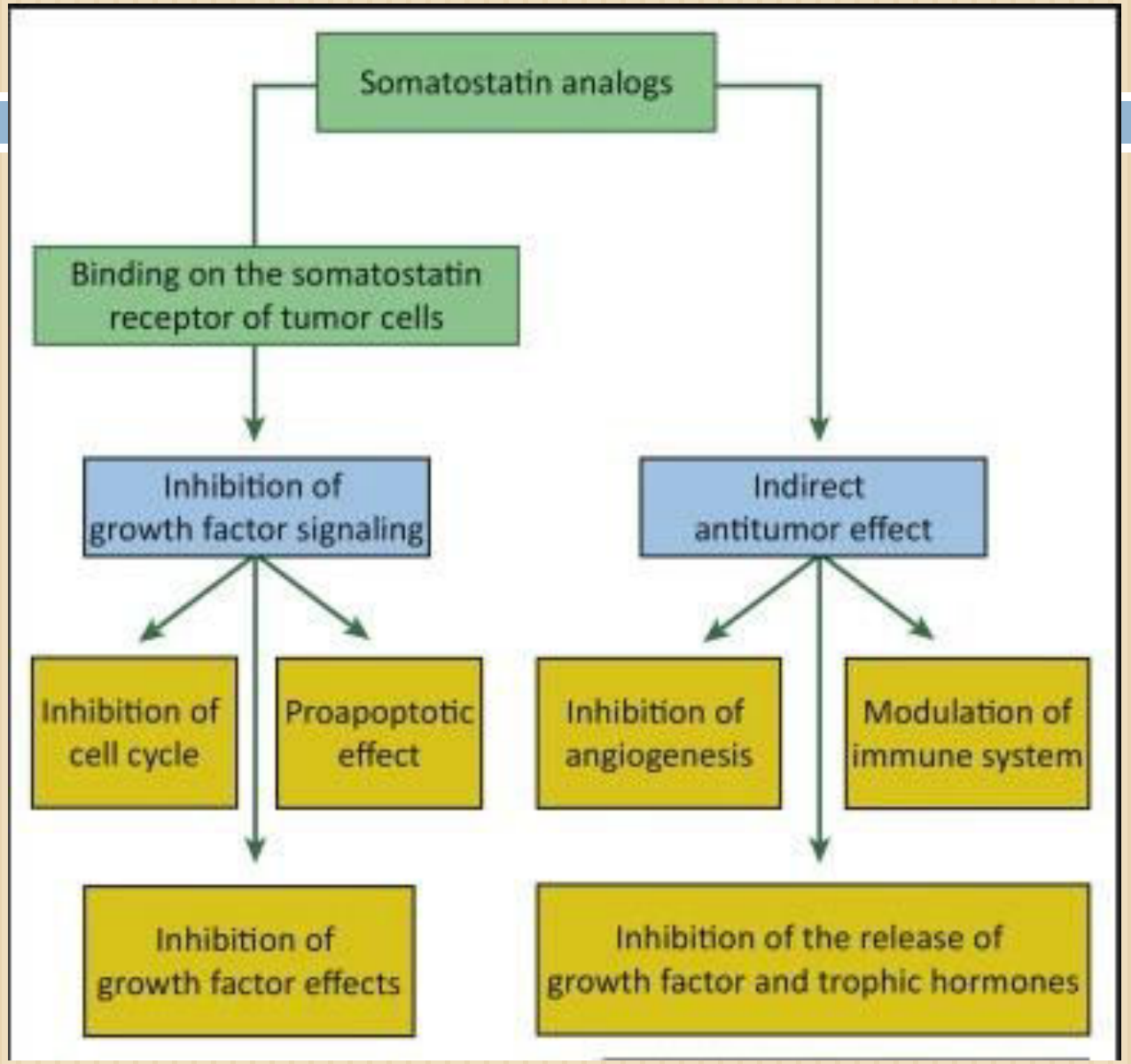
Somatostatin

- Somatostatin 14 amino acid peptide
- Found in hypothalamus, in GIT, pancreas
- Inhibit release of GH, Glucagon, Insulin, gastrin
- Somatostatin Rapidly cleared from circulation
- Half life 1-3min
- Metabolized and excreted via kidney

Octreotide



- Somatostatin analog
- Longer acting
- 45times more potent than somatostatin for inhibiting GH
- Only 2times potent than somatostatin in inhibiting insulin release so reduced chances of hyperglycemia during Octreotide treatment
- **Octreotide dosage;**
  - 50-200mcg subcutaneously 8 hourly
- **Other indication of Octreotide are**
  - Hormone secreting tumors carcinoid ,glucaganoma, gastrinoma etc
  - Diabetic diarrhea
  - Variceal bleed

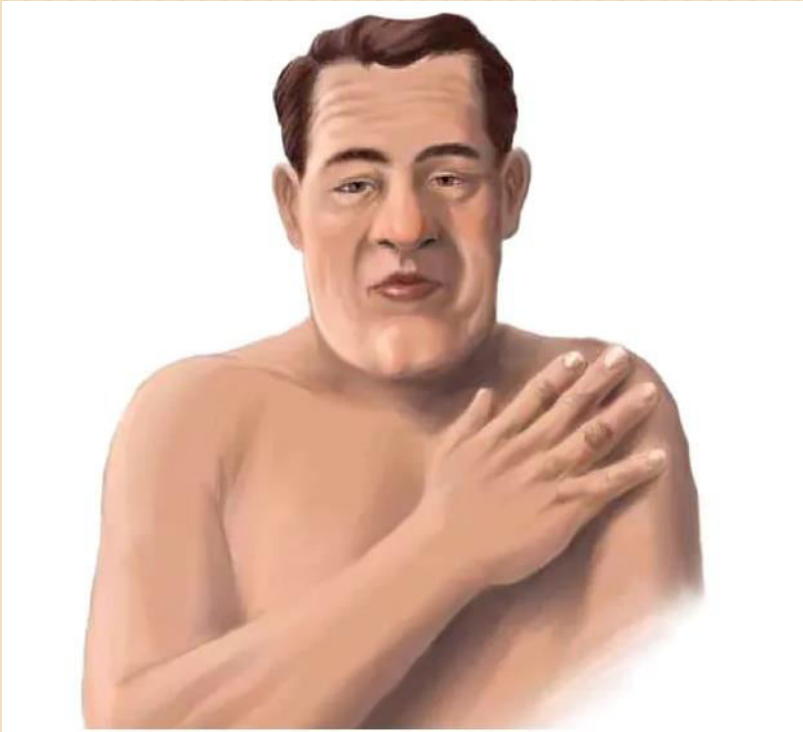

Somatostatin analogs
Binding on the somatostatin receptor of tumor cells
Inhibition of growth factor signaling
Indirect antitumor effect
Inhibition of cell cycle
Proapoptotic effect
Inhibition of angiogenesis
Modulation of immune system
Inhibition of growth factor effects
Inhibition of the release of growth factor and trophic hormones

Octreotide acetate

- Octreotide acetate
- slow release microsphere formulation
- Alternate gluteus muscle at 4week interval
- Doses of 20-40mg
- Given only when efficacy of Octreotide is proven by short acting formulation beforehand

Lanreotide

- Octapeptide somatostin anlog
- Long acting formulation
- FDA approved
- Once every 4 week
- Subcutaneous route

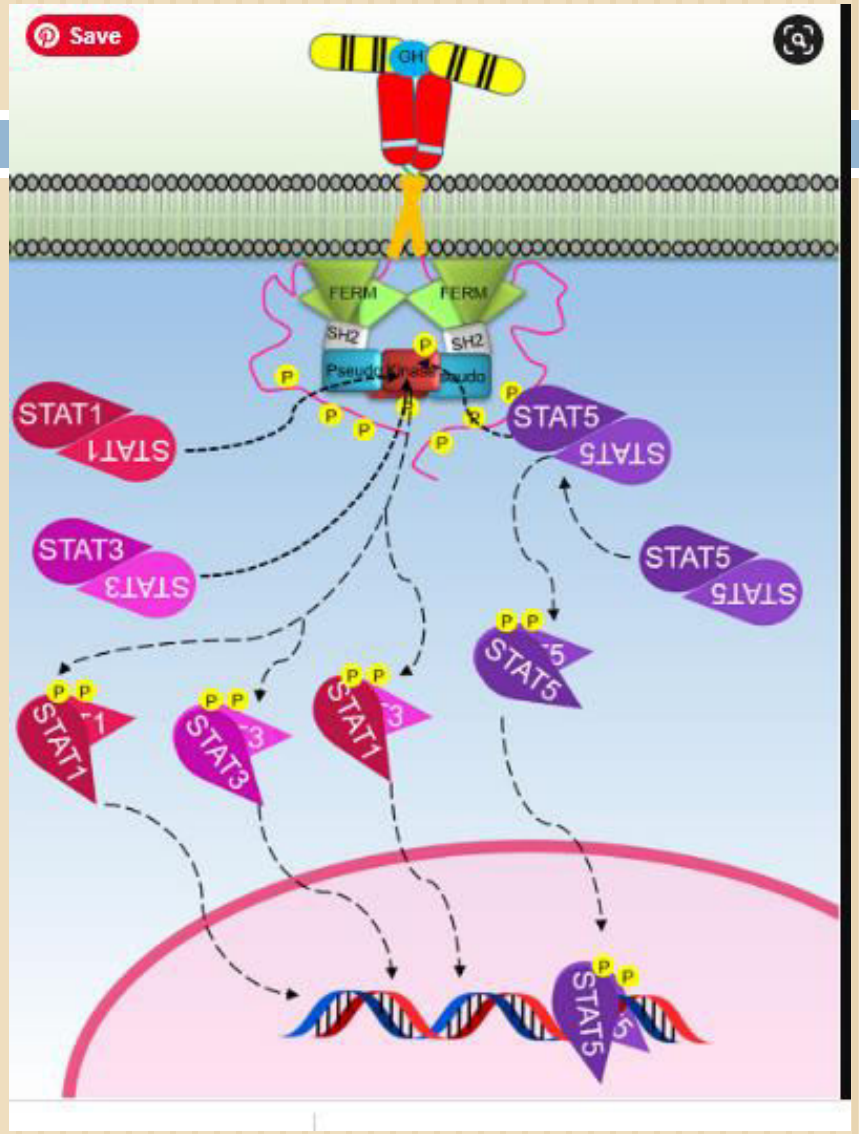


Adverse effects somatostatin analog

- Nausea vomiting, abdominal cramps, flatulence, steatorrhea, bulky bowel moments
- Biliary sludge, gallstone, gall bladder stasis
- Sinus bradycardia, and conduction disturbances
- Pain at site of injection
- Vitamin B 12 deficiency fat soluble vitamin

Pegvisomant

- GH receptor antagonist
- Used to treat acromegaly
- It is polyethylene glycol (PEG) derivative of a mutant GH, B2036
- which has increase affinity for one site of GH receptor but reduced affinity for second binding site
- Allows dimerization of receptor but blocks conformational changes required for signal transduction.
- Less potent than GH B2036 but reduced clearance due to pegylation increases its overall effectiveness
- Given subcutaneously


Save
GH
FERM
FERM
SH2
SH2
Pseudo
Pseudo
STAT1
STAT1
STAT5
STAT5
STAT3
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STAT1
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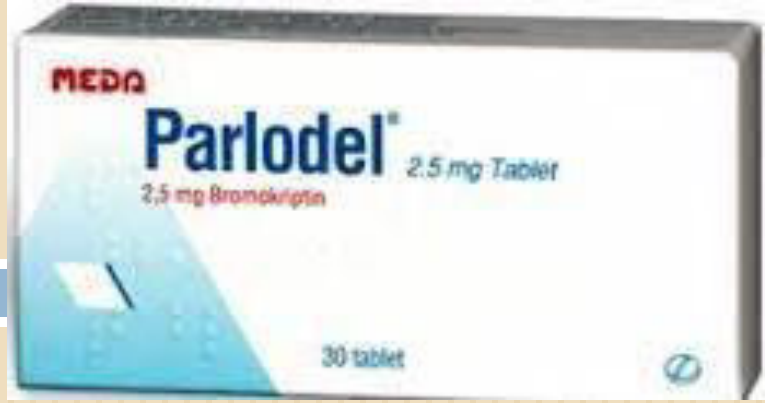
Bromocriptine



- Dopamine receptor agonists
- Ergot derivatives
- High affinity for D2 receptor
- Suppress prolactin release very effectively
- Although GH release is reduced in acromegaly but not as effectively
- Oral preparation
- Pessary form available

Bromocriptine Clinical Uses

- Prolactinoma
- Parkinson's disease
- To suppress lactation (now discouraged)
- Acromegaly
  - 20-30mg per day
  - Seldom response adequately
  - Used alone or in combination with other modality of treatment
    - Pituitary surgery
    - Radiation therapy
    - Octreotide

Toxicity adverse effects Bromocriptine

- Nausea, headache, lightheadedness
- Orthostatic hypotension, fatigue
- Psychiatric manifestation even with small doses takes longer to resolve
- Ergot derivative at high dose may cause cold induced peripheral vasospasm
- Vaginal prep causes local irritation
- Postpartum ladies may cause stroke or coronary thrombosis for suppressing lactation

Thanks

Any query ?