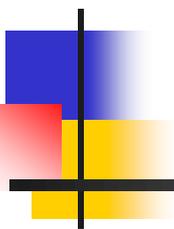
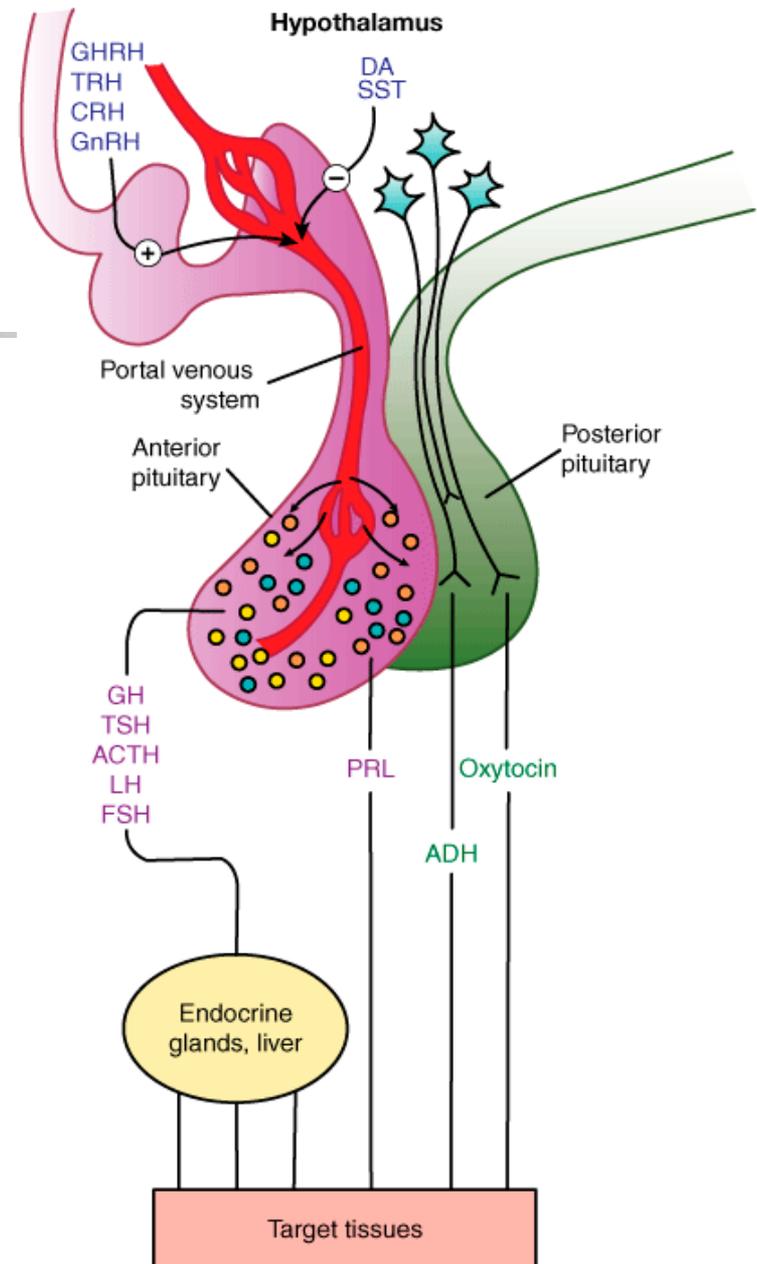


Hypothalamic & Anterior pituitary hormones



The hypothalamic-pituitary endocrine system



Source: Katzung B.G, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology*, 11th Edition: <http://www.accessmedicine.com>

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hypothalamic, anterior pituitary, and target organ hormone

Anterior Pituitary Hormone	Hypothalamic Hormone	Target Organ	Primary Target Organ Hormone or Mediator
Growth hormone (GH, somatotropin)	Growth hormone-releasing hormone (GHRH) (+) Somatostatin (-)	Liver, muscle, bone, kidney, and others	Insulin-like growth factor-1 (IGF-1)
Thyroid-stimulating hormone (TSH)	Thyrotropin-releasing hormone (TRH) (+)	Thyroid	Thyroxine, triiodothyronine
Adrenocorticotropin (ACTH)	Corticotropin-releasing hormone (CRH) (+)	Adrenal cortex	Glucocorticoids, mineralocorticoids, androgens
Follicle-stimulating hormone (FSH) Luteinizing hormone (LH)	Gonadotropin-releasing hormone (GnRH) (+) ²	Gonads	Estrogen, progesterone, testosterone
Prolactin (PRL)	Dopamine (-)	Breast	—

(+), stimulant; (-), inhibitor.

Clinical uses of hypothalamic hormones and their analogs

Hypothalamic Hormone

Clinical Uses

Growth hormone-releasing hormone (GHRH)

Used rarely as a diagnostic test for GH responsiveness

Thyrotropin-releasing hormone (TRH, protirelin)

Used rarely to diagnose hyper- or hypothyroidism

Corticotropin-releasing hormone (CRH)

Used rarely to distinguish Cushing's disease from ectopic ACTH secretion

Gonadotropin-releasing hormone (GnRH)

Used rarely in pulses to treat infertility caused by hypothalamic dysfunction

Analogues used in long-acting formulations to inhibit gonadal function in men with prostate cancer and women undergoing assisted reproductive technology (ART) or women who require ovarian suppression for a gynecological disorder

Dopamine

Analogues used for treatment of hyperprolactinemia

Diagnostic uses of thyroid-stimulating hormone and adrenocorticotropin

Hormone

Diagnostic Use

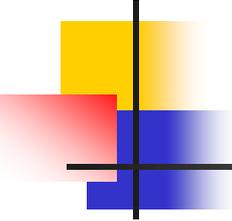
Thyroid-stimulating hormone (TSH; thyrotropin)

In patients who have been treated surgically for thyroid carcinoma, to test for recurrence by assessing TSH-stimulated whole-body ^{131}I scans and serum thyroglobulin determinations

Adrenocorticotropin (ACTH)

In patients suspected of adrenal insufficiency, to test for a cortisol response.

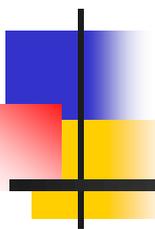
In patients suspected of congenital adrenal hyperplasia, to identify 21-hydroxylase deficiency, 11-hydroxylase deficiency, and 3β -hydroxy- Δ^5 steroid dehydrogenase deficiency, based on the steroids that accumulate in response to ACTH administration

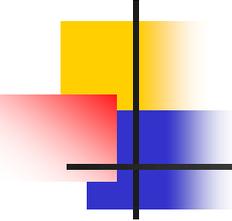


Pharmacologic Applications of hypothalamic and pituitary hormones

- Replacement therapy for hormone deficiency states
- Antagonists for diseases that result from excess production of pituitary hormones
- Diagnostic tools for identifying several endocrine abnormalities

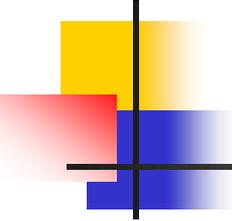
GROWTH HORMONE (SOMATOTROPIN)





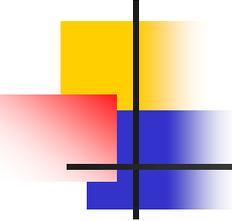
Introduction

- Peptide hormones
- Important effects on lipid and carbohydrate metabolism
- Its effects are primarily mediated via
 - **insulin-like growth factor 1 (IGF-1, somatomedin C)**
 - **insulin-like growth factor 2 (IGF-2).**



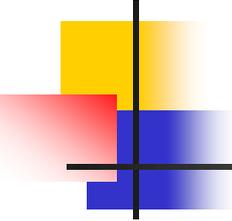
Chemistry & Pharmacokinetics

- STRUCTURE:
 - is a 191-amino-acid peptide with two sulfhydryl bridges
- rhGH
 - **Somatropin** has a 191-amino-acids
 - **Somatrem** has 192 amino acids



Pharmacodynamics

- Mediates its effects via cell surface receptors of the JAK/STAT cytokine receptor superfamily
- Has complex effects on
 - growth, body composition
 - carbohydrate, protein, and lipid metabolism
- The growth-promoting effects are mediated through IGF-1
- GH has anabolic effects in muscle and catabolic effects in lipid cells



Clinical Pharmacology

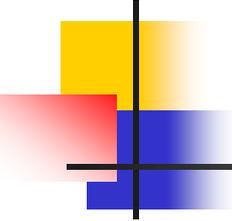
- GROWTH HORMONE DEFICIENCY
- PEDIATRIC PATIENTS WITH SHORT STATURE
- Other Uses of Growth Hormone

Clinical uses of recombinant human growth hormone

Primary Therapeutic Objective

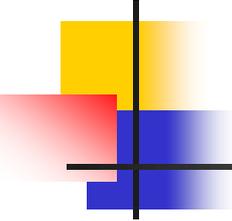
Clinical Condition

Growth	Growth failure in pediatric patients associated with: Growth hormone deficiency Chronic renal failure Prader-Willi syndrome Turner syndrome
	Small for gestational age with failure to catch up by age 2
	Idiopathic short stature in pediatric patients
Improved metabolic state, increased lean body mass, sense of well-being	Growth hormone deficiency in adults
Increased lean body mass, weight, and physical endurance	Wasting in patients with AIDS
Improved gastrointestinal function	Short bowel syndrome in patients who are also receiving specialized nutritional support



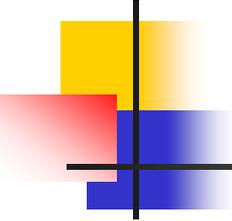
Toxicity & Contraindications

- A rarely reported side effect is intracranial hypertension, which may manifest as vision changes, headache, nausea, or vomiting



MECASERMIN

- Is a complex of
 - recombinant human IGF-1 (rhIGF-1)
 - recombinant human insulin-like growth factor-binding protein-3 (rhIGFBP-3)
- For treatment of severe IGF-1 deficiency
- The most important adverse effect is hypoglycemia



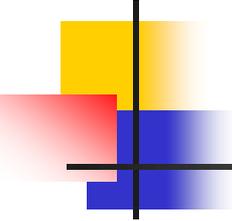
GROWTH HORMONE ANTAGONISTS

- **Somatostatin**

- It inhibits the release of
GH, glucagon, insulin, and gastrin
- has limited therapeutic usefulness

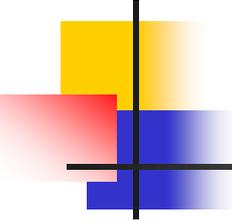
- **Octreotide**

- reduces symptoms caused by a variety of hormone-secreting tumors
 - acromegaly; the carcinoid syndrome; gastrinoma; glucagonoma; nesidioblastosis
 - the watery diarrhea, hypokalemia, and achlorhydria (WDHA) syndrome; and diabetic diarrhea.



Pegvisomant

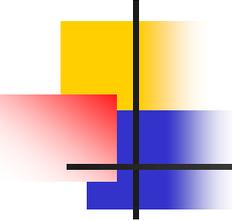
- Is a GH receptor antagonist
- Useful for the treatment of acromegaly
- The polyethylene glycol (PEG) derivative of a mutant GH, B2036,



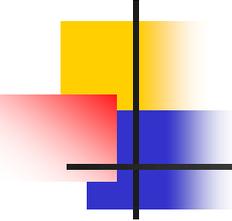
THE GONADOTROPINS

- FSH
- LH
- human Chorionic Gonadotropin (hCG)
- Are dimers that share
 - an identical α chain
 - in addition to a distinct β chain

Chemistry & Pharmacokinetics

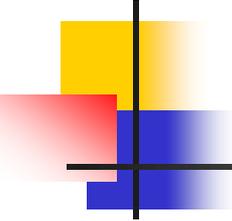


- MENOTROPINS
- FOLLICLE-STIMULATING HORMONE
 - **Urofollitropin,**
 - **follitropin alfa** and **follitropin beta**
- LUTEINIZING HORMONE
 - **Lutropin,**
- HUMAN CHORIONIC GONADOTROPIN



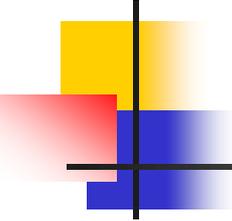
Pharmacodynamics

- Effects through G protein-coupled receptors



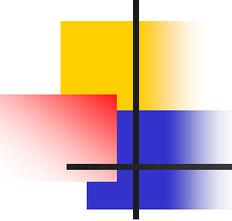
Clinical Pharmacology

- OVULATION INDUCTION
 - to induce ovulation in women with anovulation due to:
 - hypogonadotropic hypogonadism
 - polycystic ovary syndrome
 - obesity
- MALE INFERTILITY



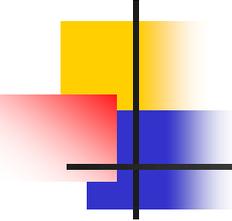
Toxicity & Contraindications

- **ovarian hyperstimulation syndrome**
- **multiple pregnancies**
- Headache, depression, edema, precocious puberty



GONADOTROPIN-RELEASING HORMONE & ITS ANALOGS

- *Pulsatile* GnRH secretion is required to stimulate the gonadotroph cell to produce and release LH and FSH
- Sustained, *nonpulsatile* administration of GnRH or GnRH analogs *inhibits* the release of FSH and LH by the pituitary



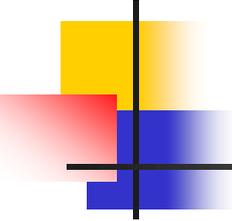
Chemistry & Pharmacokinetics

■ STRUCTURE

- GnRH is a decapeptide found in all mammals
- **Gonadorelin** is an acetate salt of synthetic human GnRH
- Synthetic analogs include **goserelin, histrelin, leuprolide, nafarelin, and triptorelin.**

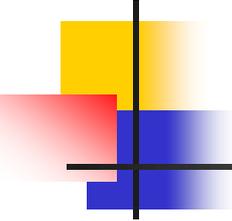
■ PHARMACOKINETICS

- GnRH analogs can be administered subcutaneously, intramuscularly, via nasal spray or as a subcutaneous implant



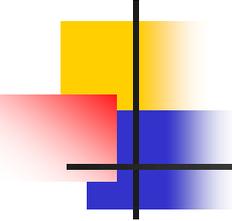
Pharmacodynamics

- GnRH exhibit complex dose-response relationships that change dramatically from the fetal period through the end of puberty.



Clinical Pharmacology

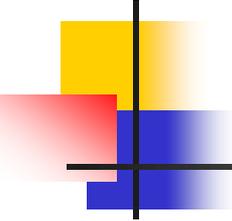
- STIMULATION
 - Female infertility
 - Male infertility
 - Diagnosis of LH responsiveness
- SUPPRESSION
 - Controlled ovarian hyperstimulation
 - Endometriosis
 - Uterine leiomyomata (uterine fibroids)
 - Prostate cancer
 - Central precocious puberty
 - Other
 - advanced breast and ovarian cancer



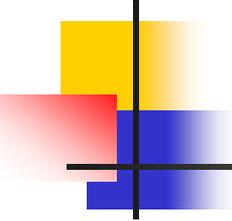
Toxicity

- Headache, light-headedness, nausea, and flushing
- Contraindications to the use of GnRH agonists in women include
 - pregnancy and breast-feeding

GNRH RECEPTOR ANTAGONISTS

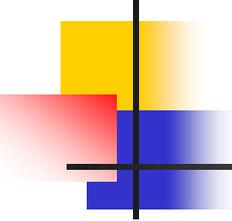


- **Ganirelix and cetrorelix**
 - Pharmacokinetics
 - absorbed rapidly after subcutaneous injection
 - Clinical Pharmacology
 - preventing the LH surge during controlled ovarian hyperstimulation
 - Toxicity
 - nausea and headache



PROLACTIN

- Is a 198-amino-acid peptide hormone
- Its structure resembles that of GH



DOPAMINE AGONISTS

- **Bromocriptine , cabergoline, pergolid and Quinagolide**
- **Pharmacokinetics**
 - All available dopamine agonists are active as oral preparations
- **Clinical Pharmacology**
 - HYPERPROLACTINEMIA
 - PHYSIOLOGIC LACTATION
 - ACROMEGALY
- **Toxicity & Contraindications**
 - **nausea, headache, light-headedness, orthostatic hypotension, and fatigue**