

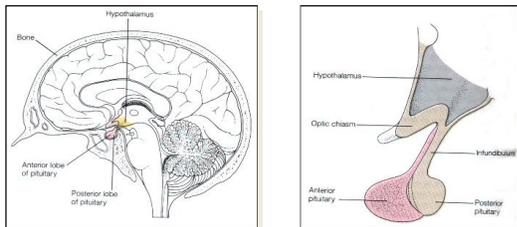
Endocrine Agents NAPNES Guidelines

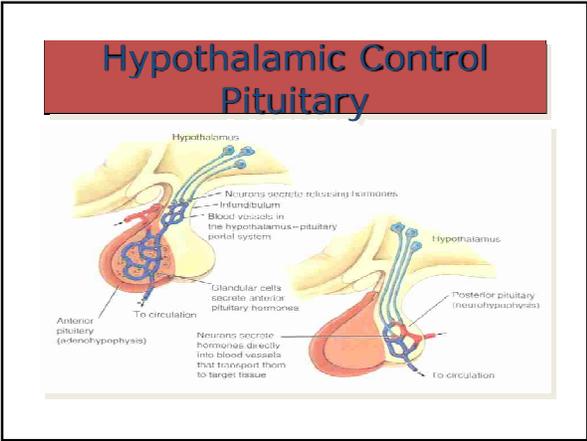
Presented by Laura Zdancewicz MSN,
CRNP

Role of the hypothalamus and pituitary gland

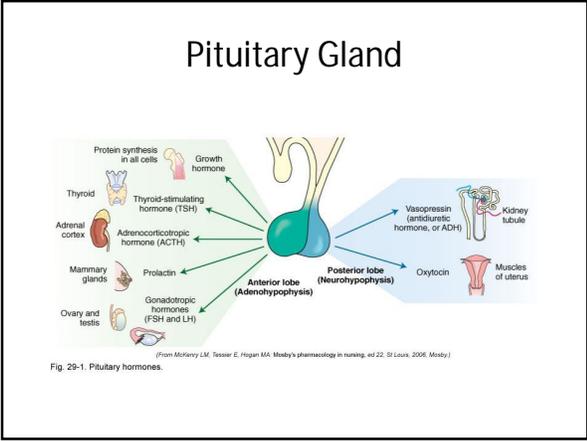
- Hypothalamus and pituitary gland
 - Two parts of the brain
 - Integrates the nervous and endocrine systems
- Hypothalamus is communication link
 - Regulates secretion of hormones by
 - Controlling the pituitary gland
- Pituitary gland releases hormones
 - Control many of endocrine system's functions

Hypothalamus





- ### Drugs related to Hypothalamic and Pituitary Function
- Anterior Pituitary
 - Growth hormone
 - Corticotropin (ACTH)
 - Thyrotropin (TSH)
 - Follicle-stimulating hormone
 - Luteinizing hormone
 - prolactin
 - Posterior Pituitary
 - Oxytocin
 - Antidiuretic hormone



Drugs related to Hypothalamic and Pituitary Function (cont.)

- Anterior Pituitary
 - Growth hormone (example – somatropin)
 - Stimulates growth in practically all tissues and organs
 - Growth hormone inhibiting factor (somatostatin)
 - Decreases growth hormone production
 - Adrenocorticotrophic hormone (example-corticotropin)
 - Acts on adrenal cortex to promote synthesis and release of adrenocortical hormones
 - Glucocorticoids
 - Mineralocorticoids
 - Androgens
 - Thyroid stimulating hormone (example – thyrotropin)
 - Acts on thyroid gland to promote synthesis and release of thyroid hormone

Drugs related to Hypothalamic and Pituitary Function (cont.)

- Anterior Pituitary (cont.)
 - Follicle-stimulating hormone (example – menotropins, gonadotropins)
 - Acts on ovaries to promote follicular growth and development
 - Promotes spermatogenesis in testes
 - Luteinizing hormone (example – gonadotropins)
 - Acts in women to promote ovulation and development of the corpus luteum
 - In men, acts on testes to promote androgen production
 - Prolactin (example-bromocriptine)
 - Stimulates milk production after parturition

Drugs related to Hypothalamic and Pituitary Function (cont.)

- Posterior pituitary
 - Oxytocin (example-pitocin, syntocinon)
 - Facilitate uterine contractions at term
 - Antidiuretic hormone - ADH (example-vasopressin)
 - Promotes renal conservation of water

Growth Hormone (GH)

- Actions
 - Promotes growth
 - Promotes protein synthesis
 - Carbohydrate metabolism
 - Stimulates liver to release glycogen for energy
- Examples
 - somatropin (Humatrope)
 - somatrem (Protopin)

Growth Hormone (cont.)

Indications

- Growth failure in children due to chronic renal insufficiency
- Growth failure in children due to deficiency of growth hormone
- Short stature associated with Turner's syndrome
- Growth hormone deficiency in adults
- Short stature
- AIDS wasting or cachexia
- Increases spinal bone density in childhood-onset growth hormone-deficient patients
- As part of a comprehensive treatment program for Short Bowel Syndrome

Growth Hormone (cont.)

- Acromegaly
 - Excess GH
 - Characterized by enlargement of many parts of the skeleton, especially the extremities
 - Coarse facial features
 - Wide hands and feet
 - Headaches
 - Excessive sweating

Growth Hormone (cont.)

- Acromegaly (cont.)
 - Treatment
 - Surgery or radiation of pituitary gland
 - Growth hormone inhibiting factor
 - somatostatin
 - sandostatin (Octreotide)
 - » Synthetic analog of somatostatin
 - » Suppresses growth hormone release
 - » Commonly used for watery diarrhea secondary to metastasis
 - Growth hormone antagonist
 - pegvisomant (Somavert)

Antidiuretic Hormone (ADH)

- Promotes renal conservation of water
- Diabetes insipidus
 - ADH deficiency
 - Polydipsia
 - Polyuria
 - Treatment
 - ADH replacement drugs
 - desmopressin (DDAVP, Stimate)
 - vasopressin (Pitressin)
 - lypressin (Diapid)

Antidiuretic Hormone (ADH)

- Other uses
 - Abdominal distention
 - Prevention/treatment of post-operative
 - Nocturnal bedwetting
 - Hemophilia A
- Adverse effects
 - Water intoxication
 - Vasoconstriction

Antidiuretic Hormone (ADH)

Adverse Effects

- CNS
 - Drowsiness, headache, lethargy
- GI
 - Nausea, heartburn, cramps
- GU
 - Uterine cramps
- CV
 - Increase BP
- Other
 - Vertigo, nasal congestion, sweating, tremors

Nursing Implications

- Obtain thorough nursing assessment, medication history
- Assess for contraindications specific to each agent

Nursing Implications

- Provide specific instructions for nasal spray forms of lypressin and vasopressin
- Rotate injection sites
- Agents should not be discontinued abruptly
- Do not take OTC products without checking with health care provider

Nursing Implications

- Parents of children who are receiving growth hormones should keep a journal reflecting the child's growth



Nursing Implications

- Monitor for therapeutic responses
 - somatropin should increase growth in children
 - desmopressin, lypressin, vasopressin should reduce severe thirst and decrease urinary output
- Monitor for side effects

Nursing Implications

- Goals of therapy of pituitary agents
 - Patient maintains a positive body image
 - Patient maintains normal fluid volume and electrolyte balance
 - Patient experiences little or no pain related to treatment
 - Most of these agents DO NOT produce a cure

Adrenocorticotrophic hormones

Adrenal Agents

Adrenocorticotrophic hormones

- Stimulate secretion of 3 types of steroid hormones from adrenal cortex
 1. Mineralocorticoids
 - Helps regulate concentration of extracellular electrolytes
 2. Glucocorticoids
 - Influence metabolism of carbohydrates, proteins & fats
 3. Sex hormones
 - Effects on sexual characteristics

Adrenocorticotrophic hormones (cont.)

- Mineralocorticoid
 - Aldosterone (naturally occurring)
 - Promotes sodium resorption in kidney
 - Pulls water and fluid along with it
 - Can lead to edema and hypertension
 - Fludrocortisone (Florinef)
 - Synthetic analog of aldosterone
 - Potent mineralocorticoid activity
 - Used in
 - Addison's disease
 - Chronic severe postural hypotension

Adrenocorticotrophic hormones (cont.)

- Glucocorticoids
 - Naturally occurring glucocorticoids
 - Hydrocortisone (cortisol)
 - Cortisone

Adrenocorticotrophic hormones
Glucocorticoids (cont.)

- Main effects
 - Inhibition of inflammatory and immune responses
 - Stabilizing the cell membrane of inflammatory cells (lysosomes)
 - Decreasing the permeability of capillaries to the inflammatory cells
 - Decreasing the migration of WBCs

Adrenocorticotrophic hormones
Glucocorticoids (cont.)

- Other effects
 - Stimulates liver to change glucose (from carbohydrates) to glycogen – *glycogenesis*
 - ↑ conversion of excess amino acids to glycogen – *gluconeogenesis*
 - ↑ use of fats for energy

Adrenocorticotrophic hormones
Glucocorticoids (cont.)

- Normal secretion
 - Limits the inflammatory process to
 - Tissue repair
 - Prevent excessive tissue destruction
- Excess secretion
 - Damaging effects
 - Decreased immune response
 - Delays healing of damaged tissue

Adrenocorticotrophic hormones
Glucocorticoids (cont.)

- Examples
 - Dexamethasone (Decadron)
 - Hydrocortisone (Cortef, Solu-cortef)
 - Prednisone (Deltasone, Orasone)
 - beclomethasone (several formulations)
 - fluticasone propionate
 - cortisone
 - Methylprednisolone
 - Many others

Adrenocorticotrophic hormones
Glucocorticoids (cont.)

- Routes available besides po:
 - By inhalation for control of steroid-responsive bronchospastic states
 - Nasally for rhinitis and to prevent the recurrence of polyps after surgical removal
 - Topically for inflammations of the eye, ear, and skin

Adrenocorticotrophic hormone (cont.)
Glucocorticoids
Side effects

- CNS
 - Convulsions, dizziness, insomnia, headache, excitatory effect on CNS leading to “steroid psychosis”
- GI
 - Nausea, vomiting, pancreatitis, increased appetite
- GU
 - Water and sodium retention, hypokalemia
- Integumentary
 - Sweating, acne, myalgia, muscle atrophy

Adrenocorticotrophic hormone (cont.)
Glucocorticoids
Side effects

- Musculoskeletal
 - Muscle breakdown
 - Weakness, reduced muscle mass/repair, myalgia
 - Reduced bone density
 - Osteoporosis, higher fracture risk, slower fracture repair
- Metabolic
 - Increased gluconeogenesis, insulin resistance, impaired glucose tolerance
 - Increased hepatic glycogen synthesis
 - Can lead to “steroid diabetes”

Adrenocorticotrophic hormone (cont.)
Glucocorticoids
Side effects

- Cushing’s Syndrome
 - Increased facial adipose tissue (moonface)
 - Increased visceral/truncal fat deposition
 - Appetite stimulation
 - Central obesity
 - Dilatation of small vessels in skin
 - Anovulation, irregular menstrual periods
 - Growth failure, pubertal delay

Adrenocorticotrophic hormone(cont.)
Side effects

- In high doses
 - Cortisol can have appreciable mineralocorticoid potency effects
 - Salt and water retention
 - Extracellular fluid volume expansion
 - Hypertension
 - Potassium depletion
 - Metabolic alkalosis

Adrenal suppression/withdrawal

- Use of high dose steroids for more than a week
 - Begins to produce suppression of the patient's adrenal glands
 - STOPS making endogenous hormone
 - The exogenous glucocorticoids suppress normal feedback mechanism
 - Prolonged suppression
 - Adrenal glands atrophy (physically shrink)
 - Can take months to recover full function after discontinuation of the exogenous glucocorticoid
- .

Prevention of Adrenal suppression/withdrawal

- If a patient has been receiving daily high doses for 5 days or less
 - Can be abruptly stopped
 - Full adrenal recovery can be assumed to occur by a week afterward
- High doses used for 6-10 days
 - Reduce to replacement dose (20mg) immediately and taper over 4 more days
 - Adrenal recovery can be assumed to occur within 2-4 weeks of completion of steroids.
- If high doses were used for >11 days
 - More prolonged tapers are needed per prescriber

Adrenocorticotrophic hormone(cont.)
Drug Interactions

- Cortisol (cont.)
 - Diuretic and Amphotericin B
 - Additive effect
 - Lowering potassium levels

Adrenocorticotrophic hormone(cont.)
Drug Interactions

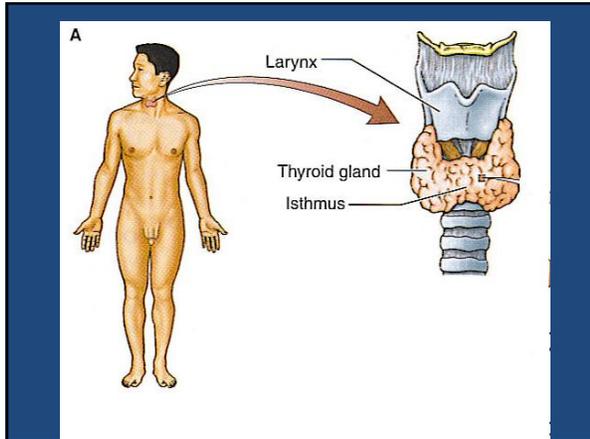
- Nursing implications
 - Monitor electrolytes (esp. K+)
 - Monitor glucose (may increase)
 - Give with food for oral doses
 - Monitor weight and blood pressure
 - Monitor for increased susceptibility to infection
 - Monitor for psychosis

Thyroid & Antithyroid Agents

Thyroid Disorders

Thyroid Gland

- Located near the parathyroid gland
- Secretes three hormones essential for proper regulation of metabolism
 - Triiodothyronine (T_3)
 - Highly active
 - Thyroxine (T_4)
 - Less active
 - Precursor to T_3
 - Calcitonin
 - Lowers serum calcium
 - Responsible for maintaining adequate levels of calcium in the extracellular fluid



Thyroid Gland

- T_3 & T_4
 - Principal actions
 - Stimulation of energy
 - Stimulation of the heart
 - Growth & development
 - \uparrow response to epinephrine



Hypothyroidism

Deficiency in Thyroid Hormones

- Primary
 - Abnormality in the thyroid gland itself
- Secondary
 - Results when the pituitary gland is dysfunctional and does not secrete TSH
- Tertiary
 - Results when the hypothalamus gland does not secrete TRH (stimulates the release of TSH)

Hypothyroidism

- Cretinism
 - Hyposecretion of thyroid hormone during youth
 - Signs and symptoms
 - low metabolic rate
 - retarded growth and sexual development
 - possibly mental retardation

Hypothyroidism



Hypothyroidism (cont'd)

- Myxedema
 - Hyposecretion of thyroid hormone as an adult
 - Signs and symptoms
 - decreased metabolic rate
 - loss of mental and physical stamina
 - weight gain
 - loss of hair
 - Brittle hair
 - firm edema
 - yellow dullness of the skin



Hypothyroidism (cont'd)

- Goiter
 - Enlargement of the thyroid gland
 - Results from over-stimulation by elevated levels of TSH
 - TSH is elevated because there is little or no thyroid hormone in circulation



Hypothyroidism (cont'd)

- Common symptoms
 - Thickened skin
 - Hair loss
 - Constipation
 - Lethargy
 - Anorexia

Thyroid Replacement Preparations

- levothyroxine (Synthroid, Levoxyl)
 - Synthetic thyroid hormone T₄
 - **Most commonly used preparation**
- liothyronine (Cytomel)
 - Synthetic thyroid hormone T₃
- liotrix (Thyrolar)
 - Synthetic thyroid hormone T₃-T₄ combined
- Thyroid
 - Desiccated (dried) animal thyroid gland

Thyroid Replacement Preparations Mechanism of Action

- Thyroid preparations are given to replace what the thyroid gland cannot produce to achieve normal thyroid levels (euthyroid)
- Thyroid drugs work the same way as thyroid hormones
- Normal dosages of levothyroxine
 - **PO (Adults):**
Hypothyroidism—50 mcg as a single dose initially; may be increased q 2–3 wk; usual maintenance dose is 75–125 mcg/day (1.5 mcg/kg/day).

Thyroid Replacement Preparations
Levothyroxine

- Half-life 7 days
 - Dosed daily
- Adverse Effects
 - Tachycardia
 - Angina
 - Tremors
 - Weight loss
 - Fever

Thyroid Replacement Preparations
Indications

- To treat all three forms of hypothyroidism
- Levothyroxine is the preferred agent
 - hormonal content is standardized
 - Its effect is predictable
- Also used for thyroid replacement in patients whose thyroid glands have been surgically removed or destroyed by radioactive iodine in the treatment of thyroid cancer or hyperthyroidism

Thyroid Replacement Preparations
Side Effects

- Most significant adverse effect
 - Cardiac dysrhythmia
- Others
 - Tachycardia, palpitations, angina,
 - hypertension, insomnia, tremors,
 - headache, anxiety, nausea, diarrhea,
 - menstrual irregularities, weight loss,
 - sweating, heat intolerance, others

Thyroid Replacement Preparations Drug Interactions

- Drug interactions
 - Oral anticoagulants
 - Increased effect of anticoagulant
 - Digitalis
 - Decreased digitalis levels
 - Cholestyramine
 - Decreased absorption of thyroid hormone and cholestyramine
 - Epinephrine
 - May induce coronary insufficiency
 - Beta-blockers
 - ↓ response of BB
 - Anti-diabetic agents
 - ↑ requirement for insulin & oral anti-diabetic agents

Hyperthyroidism: Excessive Thyroid Hormones

- Caused by several diseases
 - Graves' disease
 - Excessive thyroid hormone secretion
 - Plummer's disease (toxic nodular disease)
 - Thyroid adenoma
 - Multinodular disease
 - Thyroid storm (Thyrotoxic crisis)
 - Induced by stress or infection

Hyperthyroidism (cont.)

- Affects multiple body systems, resulting in an overall increase in metabolism
 - Diarrhea
 - Flushing
 - Increased appetite
 - Muscle weakness
 - Sleep disorders
 - Altered menstrual flow
 - Fatigue
 - Palpitations
 - Nervousness
 - Heat intolerance
 - Irritability
 - Weight loss

Hyperthyroidism

Treatment

- Radioactive iodine (I^{131})
 - Works by destroying the thyroid gland
- Surgery to remove all or part of the thyroid gland
- Antithyroid drugs: thioamide derivatives
 - methimazole (Tapazole)
 - propylthiouracil (PTU)

Tapazole & PTU

- Antithyroid drug
- Inhibits thyroid hormone synthesis
- Short half-life
- Uses
 - Grave's disease/hyperthyroidism
 - Adjunct to radiation therapy
 - Surgery
 - Thyrotoxic crisis
 - Pre-operatively
 - ↓ s/s of hyperthyroidism & ↓ thyroid vascularity

Tapazole & PTU (cont.)

Adverse Effects

- CNS
 - Drowsiness, headache, vertigo, paresthesia
- Skin
 - Rash, pruritis
- GI
 - Nausea, vomiting, diarrhea, jaundice
- Musculoskeletal
 - Myalgia, arthralgia, nocturnal muscle cramps

Tapazole & PTU (cont.)

Adverse Effects

- Hematologic
 - Leukopenia
 - Thrombocytopenia
 - Bleeding
 - Agranulocytosis
 - Within first 2 months of therapy
- Hypothyroidism
 - Occurs with excessive dosing
- Neonatal hypothyroidism
 - Crosses the placenta
 - Enters breast milk

Radioactive Iodine I¹³¹

- Radioactive isotope
- Emits gamma and beta rays
- Half-life 8 days
- Action
 - Produces clinical remission with destruction of thyroid gland

Radioactive Iodine I¹³¹

Nursing Interventions

- All anti-thyroid & thyroid preps must be stopped 1 week prior
- Institute radiation precautions
 - Urine and saliva slightly radioactive x 24h
 - Pregnant women should not care for pt
 - Disposable utensils and linens
 - Save urine for 24-48h in lead containers

Radioactive Iodine I¹³¹

Nursing Interventions

- Limit contact with patient (NO LONGER THAN NEEDED)
 - 1st day – less than 30 minutes/shift
 - 2nd day – up to one hour
 - 3rd day – may be longer

* Individual institutional policies may vary

Hyperthyroidism

Treatment: Antithyroid Agents

- Used to palliate hyperthyroidism
 - to prevent the surge in thyroid hormones that occurs after the surgical treatment or during radioactive iodine treatment for hyperthyroidism
- Cautions
 - May cause liver and bone marrow toxicity

Nursing Implications

- Assess for drug allergies, contraindications, potential drug interactions
- Obtain baseline vital signs, weight
- Cautious use
 - Cardiac disease,
 - Hypertension
 - Pregnant women

Nursing Implications

- Teach patient
 - Take thyroid agents once daily in the morning
 - Decrease the likelihood of insomnia
 - Take the medications at the same time every day
 - Not to switch brands without physician approval

Nursing Implications

- Teach patients
 - Report any unusual symptoms, chest pain, or heart palpitations
 - Not to take OTC medications without physician approval
 - Therapeutic effects may take several months to occur

Nursing Implications

- Antithyroid medications
 - Better tolerated when given with food
 - Give at the same time each day to maintain consistent blood levels
 - Never stop these medications abruptly
 - Avoid eating foods high in iodine (seafood, soy sauce, tofu, and iodized salt)

Nursing Implications

- Monitor for therapeutic response
- Monitor for side/adverse effects
 - Symptoms of overdose of thyroid hormones include
 - Cold intolerance
 - Depression
 - Edema

Diabetes Mellitus

Drug therapy

Diabetes Mellitus (DM)

- Chronic disease
 - Carbohydrate metabolism
 - Fat & protein metabolism (lesser degree)
- Inadequate production/utilization of insulin
 - Hyperglycemia
 - Glycosuria
- ~ 14.6 million people w/diagnosis
 - ~6.2 million undiagnosed

CDC statistics (2005)

Diabetes Mellitus Pathophysiology

- Glucose
 - Used for energy by cells
 - Broken down from dietary carbohydrates
 - Smaller amounts from protein & fats
- Insulin
 - Produced by islets of Langerhans (pancreas)
 - Combines with receptor on cell membrane
 - Allows glucose to enter cell
 - ↓ serum glucose
 - Allows for storage of glucose in liver
 - Form of glycogen

Diabetes Mellitus Pathophysiology

- Glucagon
 - Produced in islets of Langerhan
 - Raises blood sugar when needed
 - From storage in the liver
- Insulin & Glucagon
 - Work together
 - Maintain a normal serum glucose

Diabetes Mellitus Pathophysiology

- Diabetes Mellitus
 - Faulty production of insulin (hypoinsulinism)
 - Inability of body to utilize insulin
 - Results in **hyperglycemia**

Diabetes Mellitus Metabolic Syndrome

- Waistline
 - >40 inches – men
 - >35 – female
- BP > 130\80 or on BP meds
- Triglycerides >150mg/dl or on meds
- FBS > 100mg/dl or on meds
- HDL < 40mg/dl
- BMI >30

Types of Antidiabetic Agents

- Insulins
- Oral hypoglycemic agents

Both aim to produce normal blood
glucose states

Diabetes Mellitus Insulin

- Function as a substitute for the endogenous hormone
- Effects are the same as normal endogenous insulin
- Restores the diabetic patient's ability to:
 - Metabolize carbohydrates, fats, and proteins
 - Store glucose in the liver (as glycogen)
 - Convert glycogen to fat stores

Diabetes Mellitus

Insulin

- Type 1 DM/Latent Autoimmune Diabetes of Adulthood (LADA)
 - Produce no endogenous insulin
- Type 2 DM/Maturity Onset Diabetes of the Young (MODY)
 - If diet and/or oral hypoglycemics fail
- Cannot be given by mouth
 - Insulin is a protein
 - Digested by gastric juices
 - Broken down & inactivate
- Given subcutaneously
 - IM or IV in emergencies

Diabetes Mellitus

Insulin (cont.)

- Most common dose strength
 - U-100
- Rotate sites
 - Avoids tissue injury
- Onset of action
 - Time elapsed before glucose starts to decrease
- Peak
 - Blood glucose at lowest point
 - At risk for hypoglycemia
- Duration
 - Length of time it takes for insulin effects to cease

Diabetes Mellitus

Human-Based Insulins

Rapid acting

- Most rapid onset of action
 - Shorter duration
1. Insulin aspart (NovoLog)
 - Onset - 10"
 - Peak 1 - 3 hrs
 - Duration 3-5 hrs
 2. Insulin lispro (Humalog)
 - Onset - 15"
 - Peak 30 - 90"
 - Durations \leq 5 hrs
 3. Insulin glulisine (Apidra) - newest rapid-acting
 - Similar onset, peak and duration of the "logs"
 - Given 15" ac to 20" after starting a meal



Diabetes Mellitus Human-Based Insulins

- Short acting
 - Regular insulin (Humulin R, Novolin R)
 - The only insulin product that can be given by IV bolus, IV infusion, or even IM
 - Onset
 - » 30 – 60” (more rapid w/human than pork)
 - Peak
 - » 1 -4 hrs (more rapid w/human than pork)
 - Duration
 - » 6 -12 hrs (longer w/pork than human)

Diabetes Mellitus Human-Based Insulins

- Intermediate acting
 - Isophane insulin suspension
 - also called NPH
 - Humulin N, Novolin N
 - Insulin zinc suspension
 - also called Lente
 - Humulin L, Novolin L
 - Both have a cloudy appearance

Diabetes Mellitus Human-Based Insulins

- Intermediate acting (cont'd)
 - Slower in onset and more prolonged duration than endogenous insulin
 - Onset
 - Lente – 1 to 3 hrs
 - NPH – 1 to 2 hrs
 - Peak
 - 6 to 14 hrs
 - Duration
 - 16 to 24 hrs

Diabetes Mellitus Human-Based Insulins

- Long acting
 - Glargine (Lantus)
 - Clear, colorless solution
 - Extended insulin zinc suspension (Ultralente, Humulin U)
 - White, opaque solution

Diabetes Mellitus Human-Based Insulins

- Long acting
 - Onset
 - Lantus – 1.1 hrs
 - Humulin U – 4 to 6 hrs
 - Peak
 - Lantus – no significant peak
 - Humulin U – 8 to 20 hrs
 - Duration
 - Lantus – 24 hrs
 - Humulin U – 24 – 28 hrs (with 0.5 units/kg) – dose dependent

Diabetes Mellitus insulin detrimir (Levemir)

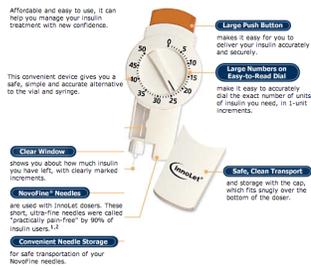
- **Long-acting basal insulin**
 - Not a human insulin
 - Made by recombinant DNA technology
 - Called a insulin analog
 - Help patients get to goal with up to 24-hour control
 - Low rate of hypoglycemia
 - Less weight gain
 - Consistent blood glucose response



Diabetes Mellitus insulin detemir (Levemir)

- Available
 - 10 ml vials
 - 3ml PenFill cartridges
 - 3ml FlexPen
 - 3ml InnoLET
- Pharmacokinetics
 - Onset – within 2 hr
 - Peak – 3 -14 hours (not significant)
 - Duration – 24 hours

InnoLet Device



Diabetes Mellitus Inhaled Insulin

- Exubera
 - Alternative to short-acting mealtime insulin
 - Fast onset (like Humalog/Novolog)
 - 10 – 20 minutes
 - Peak – 2 hours
 - Longer duration (like regular insulin)
 - 6 hours
 - Come out summer of 2006
 - Only approved for adults
 - Available in blister packs*
 - 1 mg blister = 3 units reg insulin
 - 3mg blister = 8 units reg insulin

*dosages not substitutable – due to differences in equivalents

**COMPARISON ACTIONS OF HUMAN
INSULIN & ANALOGS**

Insulin Preparation	Onset of Action	Peak Action	Duration of Action
lispro (Humalog), aspart (Novolog), glulisine (Apidra)	5 to 15 minutes	1 to 2 hours	4 to 6 hrs
human regular (Humulin R, Novolin R)	30 to 60 minutes	2 to 4 hours	6 to 10 hours
human NPH (Humulin N, Novolin N)	1 to 2 hours	4 to 12 hours	10 to 18 hours
glargine (Lantus) detemir (Levemir)	1 to 2 hours 0.8 to 2 hours	Flat Relatively flat	24 hours up to 24 hours

**ONLY A GUIDE – TIMES MAY VARY SLIGHTLY WITH
DIFFERENT SOURCES*

**Diabetes Mellitus
Human-Based Insulins**

- Premixed insulins
 - **Humulin 50/50** (50% NPH, 50% Regular), **Humulin 70/30** (70% NPH, 30% Regular), **Novolin 70/30** (70% NPH, 30% Regular), **Novolog Mix 70/30** (70% insulin aspart protamine, 30% insulin aspart), **Humalog Mix 75/25** (75% insulin lispro protamine, 25% insulin lispro)

**Diabetes Mellitus
Sliding-Scale Insulin Dosing**

- SC regular insulin doses adjusted according to blood glucose test results
 - Used during stress or hospitalization
 - Dose determined by blood glucose
 - Usually ac & hs
 - Glucose “covered” with regular (short-acting) insulin

Diabetes Mellitus
Sliding-Scale Insulin Dosing

Example of MD order:

- Sliding scale coverage
 - 70 – 150 no insulin
 - 151 – 200 2 units Humulin R
 - 201 – 350 4 units Humulin R
 - 351 – 400 6 units Humulin R
 - Over 400 call MD

Diabetes Mellitus

- Carbohydrate coverage
 - Pre-set (by MD) carbohydrate/insulin coverage
 - i.e. 15:1
 - For every 15 grams of carbohydrates-give 1 unit insulin

Diabetes Mellitus

- Insulin Sensitivity Factor/Correction Formula
 - Drop of blood glucose (mg/dl) that will occur with 1 unit of rapid acting insulin
 - Complex formula
 - Based on the patients total daily dose of insulin
 - Only useful for Type I DM
 - Done in combo with carbohydrate coverage
 - “covers” individual fluctuations of insulin response

Oral Antidiabetic Agents

- Indications
 - Used alone or in combination with other agents and/or diet and lifestyle changes to lower the blood glucose levels in patients with type 2 diabetes
- Treatment for type 2 diabetes includes lifestyle modifications
 - Diet, exercise, smoking cessation, weight loss
- Oral antidiabetic agents may not be effective unless the patient also makes behavioral or lifestyle changes

Oral Antidiabetic Agents (cont.)

- Oral hypoglycemics
 - Not oral insulin
 - Not useful for type 1 diabetics
 - Depend on some pancreas functioning
 - Stimulate beta cells of pancreas to secrete insulin
 - Can develop tolerance
 - Switch to another type
 - Eventually may no longer work
 - Pt may not be compliant with diet/exercise
 - Worsening insulin resistance
 - Insulin may become necessary
 - Pt still has type II DM
 - Insulin not needed to sustain life like in Type I DM

Oral Antidiabetic Agents (cont.)

- Sulfonylureas
 - 1st generation drugs (diabinese, tolinaise, orinase)
 - Older class
 - More side effects
 - ↑ risk of death from cardiovascular disease
 - 2nd generation (micronase, diabeta) & 3rd generation (glucotrol XL, amaryl) drugs
 - Newer classes
 - More potent
 - Fewer side effects

Oral Antidiabetic Agents (cont.)

- Sulfonylureas (cont.)
 - Mechanism of action
 - stimulate insulin production from Beta cells
 - Side effects
 - Contribute to hyperinsulinemia & weight gain
 - Insulin resistance
 - Risk of hypoglycemia
 - May cause beta cell exhaustion quicker
 - Contributing to worsening of diabetes

Oral Antidiabetic Agents (cont.)

- Biguanides – Metformin (Glucophage)
 - Mechanism of action
 - Suppresses glucose production in liver
 - Enhances peripheral tissue sensitivity to insulin
 - **Does not** stimulate pancreas to secrete insulin
 - Reduces blood glucose w/o risk of hypoglycemia
 - Often suppresses appetite – weight loss
 - ↓ triglycerides & LDL, slight ↑ HDL

Oral Antidiabetic Agents (cont.)

Biguanides – Metformin (Glucophage)

- Dose
 - 500mg – 850mg BID (morning & evening meals)
 - Can ↑ dose by 500 or 850mg q 1-2 weeks to max dose of 2550/day
- Side effects
 - Lactic acidosis – can lead to death
 - Do not use if cr > 1.5 mg/dl
- Used in combination w/sulfonylureas

Oral Antidiabetic Agents (cont.)

- Alpha-Glucosidase Inhibitors – Acarbose (Precose) & miglitol (Glyset)
 - Mechanism of action
 - Inhibits absorption of complex carbs from gut
 - No effect on glucose
 - Reduces post prandial hyperglycemia
 - Side effects
 - Flatulence
 - Abd pain
 - diarrhea

Oral Antidiabetic Agents (cont.)

- Thiazolidinediones – rosiglitazone (Avandia) & pioglitazone (Actos)
 - Mechanism of action
 - Directly enhances insulin sensitivity in skeletal muscle & adipose tissue
 - Inhibits glucose output by liver w/o causing hypoglycemia
 - Side effects
 - Associated w/liver failure
 - Monitor LFTs

Oral Antidiabetic Agents (cont.)

Thiazolidinediones: Black Box Warnings

- **Congestive Heart Failure**
 - cause or exacerbate CHF;
 - observe pts closely after tx initiation or dose incr.
 - s/sx incl. excessive, rapid wt gain, dyspnea, and/or edema;
- **Myocardial Ischemia**
 - available data inconclusive on myocardial ischemia risk



Avandia 4 mg

Oral Antidiabetic Agents (cont.)

- Nateglinide (Starlix) & repaglinide (Prandin)
 - Mechanism of action
 - Stimulate insulin secretion from beta cells
 - Similar to sulfonylureas
 - Much more rapid onset of action
 - Starts working within 15 – 30*
 - Shorter duration
 - Starlix – lasts ~ 2hrs
 - Prandin – lasts ~ 4 hrs
 - Side effects
 - hypoglycemia

Oral Antidiabetic Agents Side Effects

- Sulfonylureas
 - Hypoglycemia, hematologic effects, nausea, epigastric fullness, heartburn, many others
- Metformin
 - Abdominal bloating, nausea, cramping, diarrhea, metallic taste, reduced vitamin B12 levels

Oral Antidiabetic Agents Side Effects (cont'd)

- Alpha-glucosidase inhibitors
 - Flatulence, diarrhea, abdominal pain
- Thiazolidinediones
 - Moderate weight gain, edema, mild anemia, hepatic toxicity

Incretin Hormone

- Secreted by specific cells
 - Located in small intestine
- Released in response to food intake
 - Not released if no food intake

Incretin Mimetic Agent

- exenatide (Byetta)
 - new class of agents for the treatment of type 2 diabetes
 - Therapeutic action
 - Suppressing inappropriately elevated glucagon levels
 - Promoting satiety and reducing food intake
 - Slowing the rate of gastric emptying

*Investigational drugs (2007):
Januvia & Galvus – also work by increasing incretin.*

Incretin Mimetic Agent (cont.)

- Dosage
 - Prefilled syringes – subc injection
 - 5 or 10 mcg BID
 - Each pen contains 60 doses
 - Provides 30 days of BID dosing
 - Anytime within 1 hour before morning and evening meal

Incretin Mimetic Agent (cont.)

- Side effect
 - n/v, diarrhea
 - Dizziness, headache
 - Jittery feeling
 - Acid stomach
 - Rare reports of life-threatening pancreatitis
 - Hypoglycemia
 - When given with other antidiabetics

Incretin Mimetic Agent (cont.)

Patient teaching

- Needles are not included with the pens
- Injections are given subcutaneously
 - Upper arm, upper leg (thigh), or abdomen.
- Injections are given twice a day
 - Within 60 minutes of the morning and evening meals.
- Byetta should NOT be taken after a meal.
- If a dose is missed
 - Skip that dose
 - Take the next dose at the next prescribed time
 - Do not to double dose to make up for one missed

Incretin Mimetic Agent (cont.)

Patient teaching

- An overdose of Byetta can cause symptoms of low blood sugar
- Nausea is common when first starting Byetta
 - Decreases over time in most patients.
- The injection pen should be kept in the refrigerator but never frozen
 - Frozen pens should be discarded.
- The pen should be stored without the needle attached
 - Storing with the needle attached may allow the drug to leak or allow air into the cartridge.
- The pen should be discarded after 30 days, even if there is medication left in the cartridge

Gliptins

- Inhibit incretin breakdown
 - By interfering w/dipeptidyl peptidase -4 (DPP-4)
 - Thus ↑ incretin levels
- Sitagliptin (Januvia)
 - Dosed 100mg q day (\$4.86/pill)
- Not for type I
- Use cautiously in renal impairment
 - MD may decrease dose

Gliptins (cont.)

- Side effects
 - Rarely
 - Hypersensitivity reactions
 - Skin reactions
 - Rash, urticaria, Stevens-Johnsons
- Janumet
 - Combo of Januvia & Metformin
 - Dosed BID
 - 50/1000
 - 50/500

Symlin (pramlintide)

- Synthetic analog of human hormone amylin
 - a naturally occurring hormone that is made in the beta cells of the pancreas,
 - Helps control glucose during the post prandial period
 - Secreted in response to food intake
- Self-administered injection given prior to meals
- Adverse events (co-administered with insulin)
 - Hypoglycemia – esp within 3 hours of dose
 - Nausea – decreases with time

Symlin (pramlintide)

- **Mechanism of Action**
- Slowed gastric emptying, resulting in reduced rate of glucose absorption
- Suppressed glucagon secretion
 - Reduces postprandial hepatic glucose output
 - Decreases serum glucose
- Modulated appetite

Symlin (pramlintide)

- Reduces postprandial glucose excursions
- Reduces glucose fluctuations throughout the day
- Enhances satiety, leading to potential weight loss
- Lowers mealtime insulin requirements
- Improves A1C beyond the effect of insulin alone

Symlin (pramlintide)

SYMLIN is indicated for:

- Type 2 diabetes, as an adjunct treatment in patients who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy, with or without a concurrent sulfonylurea agent and/or metformin
- Type 1 diabetes, as an adjunct treatment in patients who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy

Symlin (pramlintide)

What patients need to know when starting SYMLIN:

- Take SYMLIN right before major meals (at least 250 Calories or 30 grams of carbohydrate)
- Begin with the starting SYMLIN dose and gradually increase the dose as directed
- When first starting SYMLIN, **reduce the amount of mealtime insulin by 50%** to reduce the chance of low blood sugar
- Nausea may occur when starting or increasing the dose of SYMLIN — but it usually does not last long
- Be patient and allow time to get the full benefit of SYMLIN

Diabetes Mellitus Agents Nursing Implications

- Before giving any drugs that alter glucose levels, obtain and document:
 - A thorough history
 - Vital signs
 - Blood glucose level
 - HgA1c
 - If indicated
 - Potential complications and drug interactions

How blood sugar self-testing results may compare with A1c test results.

The chart below shows how an average daily blood sugar number might compare to a 2-3 month A1c number.

Average* Daily Blood Sugar	A1c Level
135	6%
170	7%
205	8%
240	9%
275	10%
310	11%
345	12%

*Average is based on readings taken before and after meals and at bedtime.

Achieving an A1c goal of 7% or less is essential, since every 1% increase above 6% elevates the risk of diabetes complications such as stroke, heart attack, blindness and loss of limbs.

Diabetes Mellitus Agents

Nursing Implications

- Before giving any drugs that alter glucose levels:
 - Assess the patient's ability to consume food
 - Assess for nausea or vomiting
 - Hypoglycemia may be a problem if antidiabetic agents are given and the patient does not eat
 - If a patient is NPO for a test or procedure, consult physician to clarify orders for antidiabetic drug therapy

Diabetes Mellitus Agents

Nursing Implications

- Keep in mind that overall concerns for any diabetic patient increase when the patient:
 - Is under stress
 - Has an infection
 - Has an illness or trauma
 - Is pregnant

Diabetes Mellitus Agents

Nursing Implications

- Thorough patient education is essential regarding:
 - Disease process
 - Diet and exercise recommendations
 - Self-administration of insulin or oral agents
 - Potential complications

Diabetes Mellitus Agents

Nursing Implications

- When insulin is ordered, ensure:
 - Correct route
 - Correct type of insulin
 - Timing of the dose
 - Correct dosage
- Insulin order and prepared dosages are second-checked with another nurse

Diabetes Mellitus Agents

Nursing Implications

- Insulin
 - Check blood glucose level before giving insulin
 - Roll vials between hands instead of shaking them to mix suspensions
 - Ensure correct storage of insulin vials
 - ONLY insulin syringes, calibrated in units, are to be used to measure and give insulin
 - Ensure correct timing of insulin dose with meals

Diabetes Mellitus Agents

Nursing Implications

- Insulin (cont'd)
 - When drawing up two types of insulin in one syringe, always withdraw the regular insulin first
 - Provide thorough patient education regarding self-administration of insulin injections, including timing of doses, monitoring blood glucoses, and injection site rotations

Diabetes Mellitus Agents

Nursing Implications

- Oral antidiabetic agents
 - Always check blood glucose levels before giving
 - Usually given 30 minutes before meals
 - Alpha-glucosidase inhibitors are given with the first bite of each main meal
 - metformin is taken with meals to reduce GI effects

Diabetes Mellitus Agents

Nursing Implications

- Assess for signs of hypoglycemia
- If hypoglycemia occurs:
 - Give glucagon
 - Have the patient eat glucose tablets or gel, corn syrup, honey, fruit juice or nondiet soft drink
 - Or have the patient eat a small snack such as crackers or half a sandwich
 - Monitor blood glucose levels

Diabetes Mellitus Agents

Nursing Implications

- Monitor for therapeutic response
 - Decrease in blood glucose levels to the level prescribed by physician
 - Measure hemoglobin A_{1c} to monitor long-term compliance to diet and drug therapy
 - Watch for hypoglycemia and hyperglycemia

Glucose elevating drugs

- Glucagon
 - Synthetic preparation of natural hormone
 - Dosage & Route
 - 1mg (may be repeated in 15 mins if needed) IV, IM, SC
- diazoxide (Proglycem)
 - Inhibits insulin release from pancreas
 - Commonly used for islet cell cancer or other long-term diseases that cause hypoglycemia

Glucose elevating drugs

- Oral forms
 - Concentrated glucose for self administration
 - Rapidly dissolving buccal tablets
 - Semisolid gel
 - Oral
 - buccal
