

TOPIC 10: THYROID AND REPRODUCTIVE HORMONES

I. Objectives

- A. Learn how thyroid functions & how body is affected
- B. Learn about male and female reproductive cycles
- C. Use these systems to understand the complexity of endocrine regulation

II. Thyroid hormones

- A. Role of thyroid hormones in body (Fig 6.1)
 1. Help regulate metabolic rate
 2. Help regulate growth and development in preadults
 3. Required for normal CNS activity in adults
- B. T3 and T4 Synthesis in Thyroid Gland (Fig 21.16b)
 1. Thyroid hormones produced from the amino acid tyrosine and from iodine
 - a) T3: triiodothyronine (triiodo means 3 iodine)
 - b) T4: tetraiodothyronine (tetraiodo means 4 iodine)
 2. Tyrosine, an amino acid, is synthesized by body
 3. Iodine must be ingested
 - a) actively transported against steep concentration gradient into thyroid gland.
 4. T3 and T4 synthesized and stored in the thyroid gland
- C. T3 and T4 release and transport
 1. 90% of thyroid hormone released is T4, BUT
 2. T3 is 4 times more functionally potent than T4
 3. Most of secreted T4 is converted to T3 by target cells
 4. thus T3 is more active form, but more T4 made by thyroid; this likely represents another level of control and regulation
 5. More than 99% of the T3 and T4 in blood are bound to plasma proteins (remember that thyroid hormones are lipophilic)
- D. Effects of T3 and T4
 1. Tends to be slow acting; takes hours or days to see effects. Tends to be steady levels in plasma; not much daily variation.
 2. Metabolic Rate: Increases
 3. Heat Production: Increases
 4. Intermediary metabolism: Complex. But in general, high levels of T3 and T4 tend to favor consumption, rather than storage, of fuel
 5. Sympathetic nervous system
 - a) increases the response of target cells to epi and norepi, probably by causing a proliferation of receptors on membranes of target cells.
 6. Cardiovascular system: increases heart rate and force of contraction and causes increased peripheral vasodilation to carry extra heat to body surface
 7. Stimulates growth hormone secretion, and synthesis of structural proteins and skeletal muscle.
 8. Required for CNS development, and CNS function in adults.
- E. Regulation of thyroid function (Fig 21.17)
 1. Hypothalamus secretes Thyrotropin Releasing Hormone (TRH)

- a) Note: factors which regulate production of TRH by hypothalamus are not understood very well. Stress is known to lower TRH production, and cold in infants is known to stimulate TRH production; otherwise, not well understood
 - 2. TRH stimulates anterior pituitary to produce Thyroid Stimulating Hormone (TSH)
 - 3. TSH stimulates thyroid to produce T3 and T4.
 - 4. Increased T3 and T4 negatively feedback to reduce TRH & TSH production (T4 provides stronger negative feedback).
- F. Abnormalities of thyroid function
- 1. Hypothyroidism in adult
 - a) Caused by
 - (1) primary failure of thyroid gland
 - (2) deficiency of TRH and/or TSH
 - (3) inadequate iodine supply in diet
 - b) Effects: reduced BMR; poor cold tolerance; tendency to gain weight; easily fatigued; slow weak pulse; slow reflexes & diminished alertness; slow speech, poor memory
 - c) Treatment: replacement therapy (hormone or iodine)
 - 2. Hypothyroidism from birth
 - a) Normal growth and development of CNS impaired
 - b) leads to dwarfism and cretinism
 - c) replacement therapy works only if started immediately
 - 3. Hyperthyroidism: Grave's Disease
 - a) Thyroid stimulating immunoglobulin produced by immune system
 - b) Stimulates thyroid so it releases too much T3 and T4
 - c) Leads to: excessive heat production; poor heat tolerance; increased food intake; drop in body mass; cardiovascular abnormalities; bulging eyes
 - d) Treatment: destroy the thyroid gland, give replacement T3 and T4
- III. Male Reproductive Control (Fig 22.6)
- A. GnRH from hypothalamus stimulates ant pituitary to release LH and FSH
 - 1. neural input to hypothalamus altered at start of puberty that causes GnRH to be released; not well understood
 - 2. consistent release continues, peaking in the 20's and then slowly declining
 - B. FSH directly stimulates sperm production and release of inhibin by Sertoli cells in testes.
 - C. LH stimulates release of testosterone in Leydig cells in testes
 - D. Testosterone stimulates secondary sex characteristics + also stimulates sperm production and inhibin secretion by Sertoli cells
 - E. Inhibin negatively feeds back on FSH production; testosterone negatively feeds back on GnRH production and also negatively feedbacks on LH and FSH production by pituitary
 - F. Note: small but functionally significant amounts of estrogen produced in males
- IV. Human Female Reproductive Cycle (Figs 22.13 to 22.18) (note: timing is average)
- A. Basic Anatomy: ovary, uterine tube, uterus, endometrium, cervix (Fig 22.13)

- B. Basic Events
 - 1. Ovarian Cycle
 - a) Follicular phase days 1 to 14: menstruation to ovulation
 - b) Luteal phase days 15 to 28: ovulation to just prior to menstruation
 - 2. Uterine Cycle
 - a) Menstrual phase days 1 to ~ 5: menstruation
 - b) Proliferative phase days ~5 to 14: menstruation to ovulation
 - c) Secretory phase days 15 to 28: ovulation to just prior to menstruation
- C. Early Follicular phase (days 1 to 5)
 - 1. Endometrial lining from prior cycle being shed = menstruation
 - 2. Estrogen and progesterone low & declining as part of menstruation = minimal negative feedback on hypothalamus and pituitary which allows GnRH release
 - 3. GnRH from hypothalamus stimulates ant pituitary to release LH and FSH
 - 4. FSH stimulates follicle growth (follicle contains oocyte = egg)
 - 5. LH stimulates estrogen production by growing follicle
- D. Mid Follicular phase (days 6 to 13)
 - 1. Uterus enters proliferative phase: preparation for pregnancy
 - 2. Growing follicle secretes high levels of estrogen
 - 3. Estrogen causes: endometrium (lining of uterus) to thicken in preparation for embryo implantation; follicle development; proliferation of LH receptors on follicle.
 - 4. High levels of estrogen negatively feedback on hypothalamus and pituitary, stopping rise in plasma LH; plasma FSH actually declines in response to increased estrogen and inhibin
- E. Late Follicular phase (days 13 and 14)
 - 1. For reasons that are not understood, the continued sharp rise in estrogen now *stimulates* GnRH release and LH and FSH release. This is now a positive feedback loop!!!
 - 2. Follicle now has LH receptors that have been induced by estrogen and can respond to LH
 - 3. High LH completes follicle development in ~ 18 hours
 - 4. Ovulation occurs on day 14; the oocyte released as follicle ruptures
- F. Luteal phase (days 15 to 28)
 - 1. Uterus enters secretory phase
 - 2. LH stimulates remains of follicular tissue to begin to form corpus luteum
 - 3. Estrogen levels temporarily drop because follicle no longer releasing it and corpus luteum not yet producing it.
 - 4. Drop in estrogen causes drop in LH & FSH.
 - 5. Corpus luteum begins to secrete estrogens and progesterone, maxing about 8 to 10 days after ovulation
 - 6. Progesterone negatively feedback on hypothalamus and pituitary further inhibiting secretion of LH and FSH; inhibin also reduces FSH release
 - 7. Estrogen and progesterone maintain and further vascularize the endometrium in preparation for embryo arrival

8. Assuming pregnancy does not occur, at end of luteal phase corpus luteum disintegrates and estrogen and progesterone levels drop, allowing LH and FSH secretion again, thereby initiating follicular phase of next cycle
9. Drop in estrogen & progesterone causes endometrium to disintegrate = menstruation

V. Human Gestation (38 weeks from conception; 40 weeks from end of last menstrual cycle)

- A. The first week (fig 22.20)
 1. Fertilization
 - a) occurs in oviduct
 - b) only about 0.001% of sperm make it that far; takes them an hour
 - c) cleavage begins about 24 hours after fertilization
 2. blastocyst implants (about 100 cells at this point) around day 6
 3. then extraembryonic membranes begin to develop
- B. The first trimester (months 1 to 3)
 1. Embryo secretes human chorionic gonadotropin (HCG) (Fig 22.23)
 - a) Acts like LH
 - b) Maintains progesterone and estrogen secretion by corpus luteum
 - c) This is hormone that is detected by pregnancy kits
 2. Endometrium grows over blastocyst and embryo obtains nutrients from it for 2 to 4 weeks (Fig 22.21)
 3. tissues grow out from embryo and mix with endometrium to form placenta
 - a) placenta contains maternal and embryo blood vessels = site of exchange of nutrients and wastes (Fig 22.22)
- C. The second trimester (months 4 to 6)
 1. corpus luteum deteriorates, and HCG declines (Fig 22.23)
 2. placenta secretes its own progesterone and estrogen which maintain pregnancy
 3. rapid growth of fetus
 4. fetus becomes very active
- D. The third trimester (months 7 to 9)
 1. fetus grows to 3 to 3.5 kg
 2. placenta reaches max size of nearly 1 kg
 3. estrogen levels high & trigger formation of oxytocin receptors on uterus
- E. Birth (Fig 22.24)
 1. oxytocin released by fetus and mother
 2. stimulates contractions of uterus
 3. stimulates placenta to release prostaglandins which enhance contractions
 4. contractions stimulate release of more oxytocin and prostaglandins = positive feedback loop
 5. Stages of Labor
 - a) One: opening up and thinning of cervix (dilation and effacement)
 - (1) Can last a long time
 - b) Two: expulsion of baby
 - (1) If goes on > 2 hours MDs tend to do c-section
 - c) Three: expulsion of placenta
 - (1) Comes out very soon after baby