HYPOTHALAMO-PITUITARY-OVARIAN AXIS

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REPRODUCTIVE HEALTH

Overview

- Introduction
- Components
- Secretions
- Regulation
- Functional changes with age

Definition

- System responsible for regulation of reproductive function in human female
- Involves regulatory mechanisms that coordinate and control hormone production from hypothalamus, pituitary, ovary via feedback mechanisms
- Hormone production goes hand in hand with gamete maturation and preparation for implantation

Components 1- Hypothalamus

- Part of mid-brain , lies on base of skull – beneath 3rd ventricle, anterior to Pons, posterior to optic chiasma
- Has neural connections to : Cerebral cortex, Amygdala, Hippocampus gyrus, Thalamus, Pons, Pituitary gland
- Responsible for GnRH production
- Emotional and environmental factors can affect GnRH production

Components 2: Pituitary gland

- Projection from under surface of Hypothalamus – attached via a stalk
- Anterior Pituitary – Adenohypophysis
- Posterior Pituitary – Neurohypophysis
- Hypophyseal portal circulation connects hypothalamus to adenohypophysis
- Direct neural connection to neurohypophysis
- Pituitary secretions released into general circulation – target organs

Component 3: Ovary

- Solid organ – central medulla, peripheral cortex
- Cortical stroma with graffian follicles at various stages of development
- Granulosa and Theca cells surround maturing ova in follicles

Secretions of Hypothalamus

- Releasing and inhibiting hormones that act on anterior Pituitary:
  - GnRH
  - Prolactin inhibitory factor
  - Thyrotrophin releasing hormone
  - Growth hormone releasing hormone
  - Corticotrophin releasing hormone
  - Melanocyte releasing factor
- Vasopressin and Oxytocin released via posterior pituitary

Gonadotrophin releasing hormone

- A decapeptide hormone
- Produced in pulsatile fashion – varying frequencies and amplitude at different times of menstrual cycle
- Short half-life : 2-4 min.
- Causes down regulation (desensitization) of receptors on continuous application, up-regulation with intermittent application
- Varying frequencies and amplitude determine whether FSH or LH produced

Control of GnRH secretion

- Local control by neurotransmitters and neuromodulators
  - Neurotransmitters: Dopamine, Serotonin, Norepinephrine
  - Neuromodulators: endogenous opioids (endorphins, encephalins, dynorphins), prostaglandins, peptides (activin, inhibin, follistatin)
- Feedback – ultra-short, short and long loop

Pituitary secretions

- Anterior pituitary has 2 cell types:
  - Chromophobes – act as parent cells
  - Chromophils – acidophils and basophils
- Acidophils (α cells): produce growth hormone, prolactin
- Basophils (β cells) - 3 sub-types based on shape/granules:
  - Oval – FSH, LH; angular – thyrotrophin; lightly granulated - corticotrophin

Control of FSH, LH secretion

- GnRH causes synthesis and release of both
- Both secreted from β-cells – in pulsatile fashion in response to GnRH
- Low pulse frequencies favor FSH and higher frequencies LH
- Ovarian hormones also contribute to cyclic pattern of both
- High estrogen levels induce LH production via positive feed back

Functions of FSH

- Responsible for:
  - Growth and maturation of follicles
  - Synthesis of its own receptors in granulosa cells
  - Synthesis of LH receptors in granulosa and theca cells
  - Aromatization of androgens to estrogens in granulosa cells

Functions of LH

- Androgen production in theca cells
- Luteinization of granulosa cells to secrete progesterone
- Synthesis of local prostaglandins
- Physical act of ovulation

Effects of estrogen

- Negative feed back on FSH release acting at both Pituitary and Hypothalamus
- In high levels of > 200 pg/ml, it has a positive feed back on LH production – but only in absence of progesterone
- Positive feed back usually short lived due to rising progesterone levels

Changes in axis with age

- Present and functional from 20 weeks of fetal life
- Responsible for development of primordial follicles in the fetus
- Prior to puberty, hypothalamus very much sensitive to -ve feedback by even the small amount of adrenal steroids
- Towards puberty, adrenal androgens gradually increase leading to a rise in GnRH pulses, increasing sensitivity to positive feedback of estrogen on LH

Changes continued

- Increasing GnRH – higher FSH, estrogens – thelarche, growth spurt, and eventually menarche
- Full feedback response achieved some time after menarche thus initial cycles are anovulatory
- Adrenal androgens responsible for pubic and axillary hair hence adrenarche –(8-10 yrs)

Changes with pregnancy and pill use

- Estrogen very high – very low levels of GnRH
- Immediate postpartum – Pituitary refractory to rising levels of GnRH
- High Prolactin levels – ovary less responsive to the already low levels of FSH
- With resumption of ovarian activity, prolactin may cause a short luteal phase – reduced fertility

Changes at menopause

- Ovarian follicles become resistant to pituitary hormones – low estrogen
- Levels of FSH, LH rise
- Reduced Inhibin production from ovaries also contributes
- As aging progresses, GnRH, FSH/LH production reduces despite the low estrogen