[lecture 3]

Investigations of infertility

Biochemistry Team

Teams

The Objectives

- Comprehend the laboratory approach to infertility in female
- interpret results of investigation of infertility in female
- Understand the diagnostic approach to infertility in male
- interpret results of investigation of infertility in male

Red = Import-ant

Blue = explain

Green = addition notes

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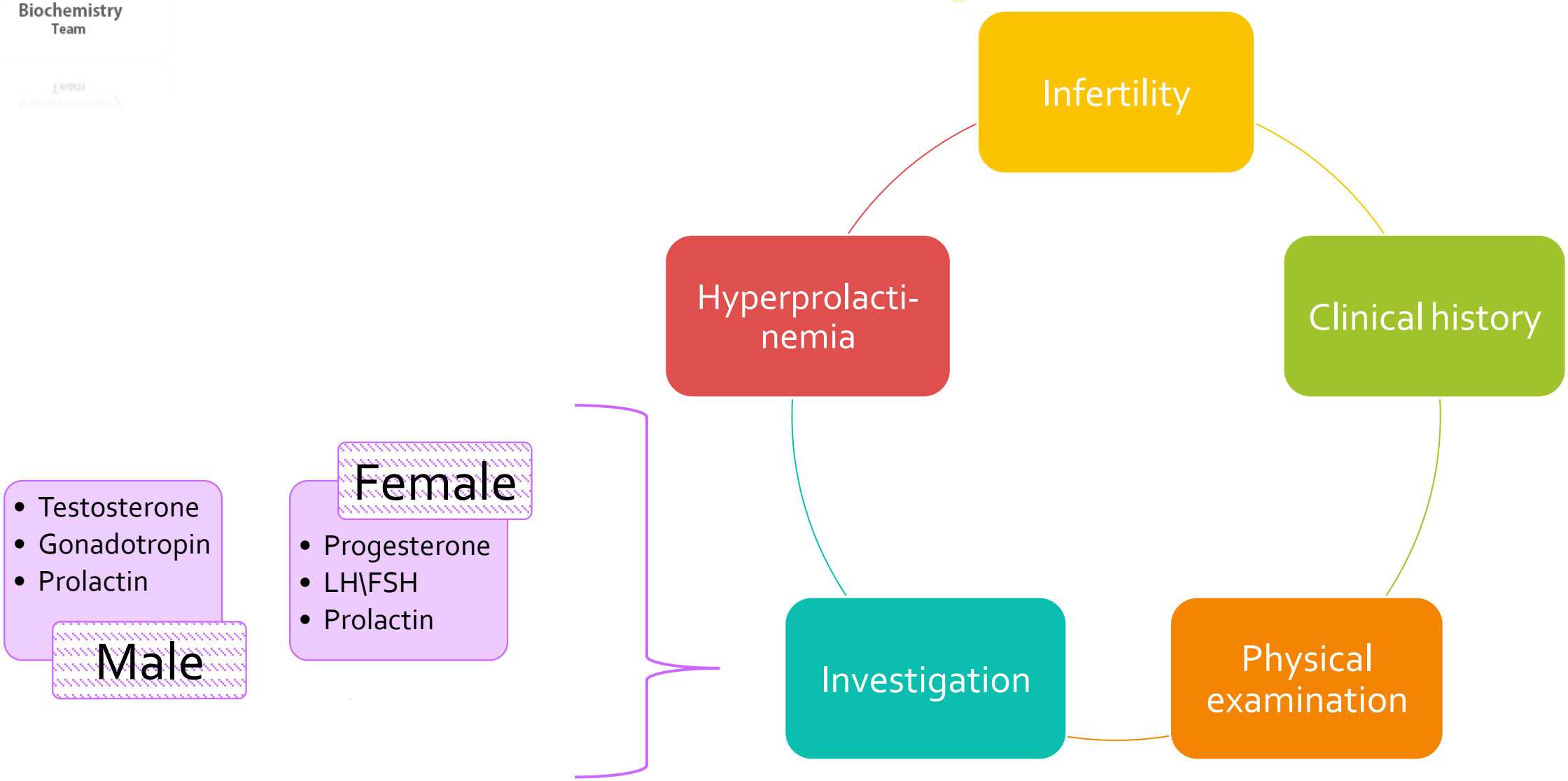
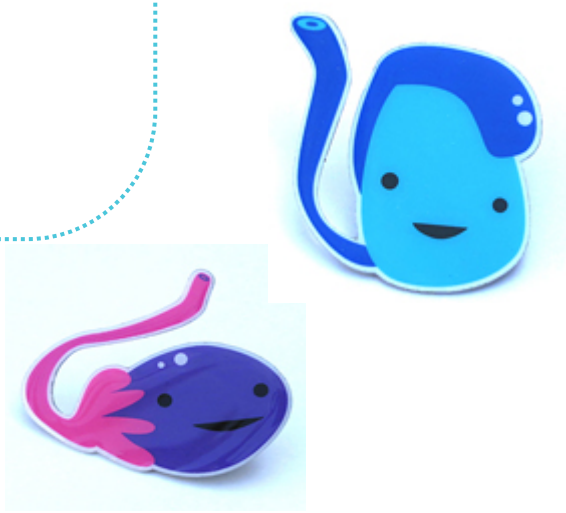
Mind Map

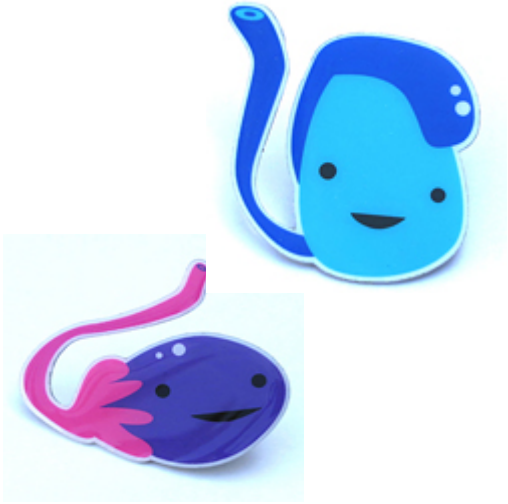

Infertility
Clinical history
Physical examination
Investigation
Hyperprolacti-nemia
Female
Progesterone
LH\FSH
Prolactin
Male
Testosterone
Gonadotropin
Prolactin

Infertility :

- **Infertility**:- Failure of a couple to conceive **after 1 year** of regular, unprotected intercourse
- Infertility may be caused by endocrine problems:
  - This is **common in the female**
  - But **rare in the male**
- Elevated serum [progesterone] **at day 21** of the menstrual cycle indicates that **ovulation has occurred**
- In both men & women infertility, a serum [FSH] > 25U/L indicates **primary gonadal failure**



Clinical history & physical examination:



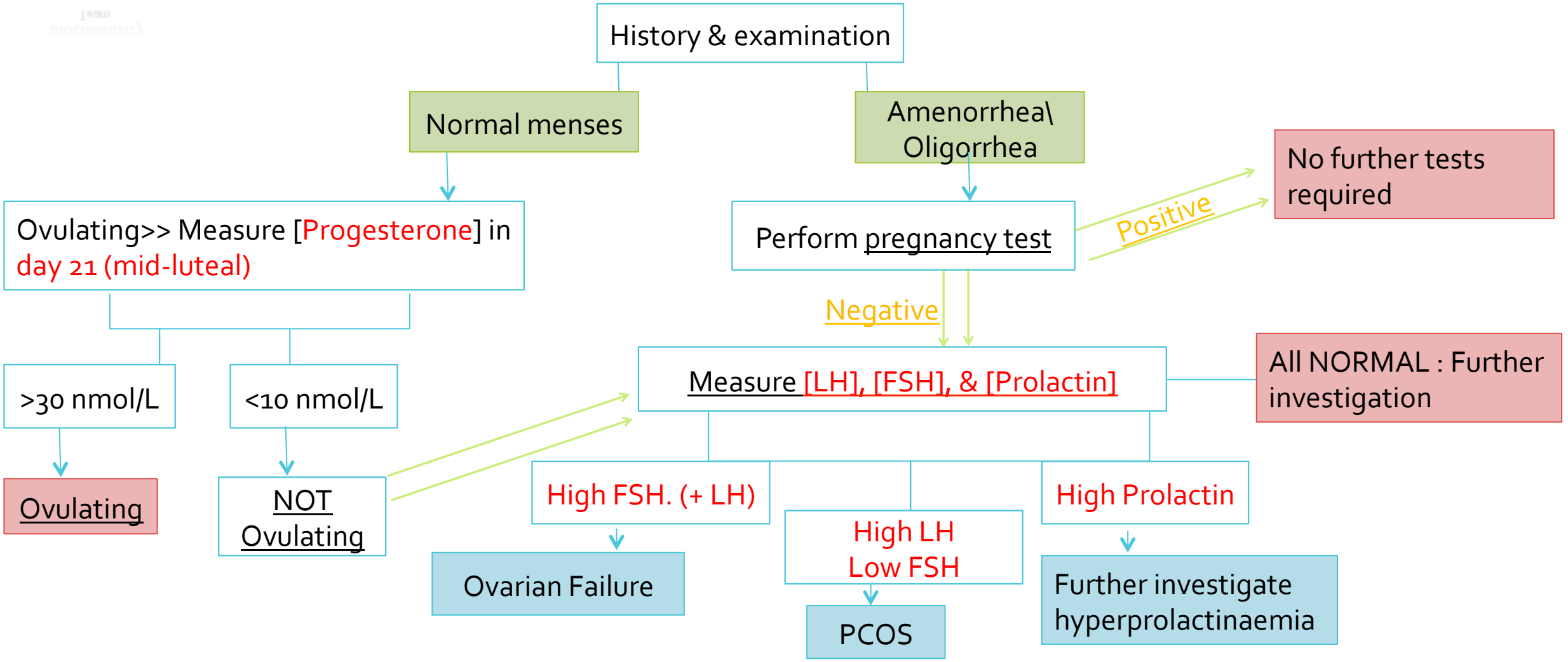
Should be **full clinical history**
Before physical examinations Information about:

- ✓ Previous pregnancies (**to know if it is secondary infertility or primary**)
- ✓ Contraceptive practice
- ✓ Serious illnesses
- ✓ Past chemotherapy or radiotherapy
- ✓ Congenital abnormalities
- ✓ Smoking habits
- ✓ Drug usage
- ✓ STD
- ✓ Frequency of intercourse

Physical examination :-
Should look for indications of:

- ✓ Hypothalamic-pituitary or thyroid disorders
- ✓ Cushing's syndrome
- ✓ **Galactorrhoea** (inappropriate breast milk production; i.e. in the absence of pregnancy most commonly caused by **hyperprolactinaemia**)
- ✓ Hirsutism (an increase in body hair with male pattern distribution)

Diagnostic approach to infertility in the woman:



Endocrine causes of infertility in women:

- **High ovarian androgen secretion:**
  - e.g.: obesity >> Insulin resistance >> ↑ ovarian androgen secretion)
- **Primary ovarian failure:**
  - postmenoposal hormonal pattern: (↑ gonadotrophins & ↓ oestradiol)
  - Hormone replacement therapy can be given (this will not treat the infertility)
- **Hyperprolactinaemia** (will be discussed)
- **PCOS:**
  - High serum [LH]
  - Normal (or low) [FSH]
- **Cushing's syndrome**
- **Hypogonadotrophic hypogonadism:**
  - Rare
  - due to hypothalamicpituitary lesion

Diagnosis of PCOS:-

In 2003, the European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) recommended that at least 2 of the following 3 features are required for PCOS to be diagnosed:

- ✓ **Oligo-ovulation or anovulation** manifested as oligomenorrhea or amenorrhea
- ✓ **Hyperandrogenism** (clinical evidence of androgen excess) or **hyperandrogenemia** (biochemical evidence of androgen excess)
- ✓ **Polycystic ovaries** (as defined on ultrasonography)

Diagnostic approach to subfertility in the man:

History & examination

Normal sperm analysis, eugonadal

endocrine tests are required

Abnormal sperm count

Measure testosterone, gonadotrophins and Prolactin

↓ Testosterone
↑ Gonadotrophins

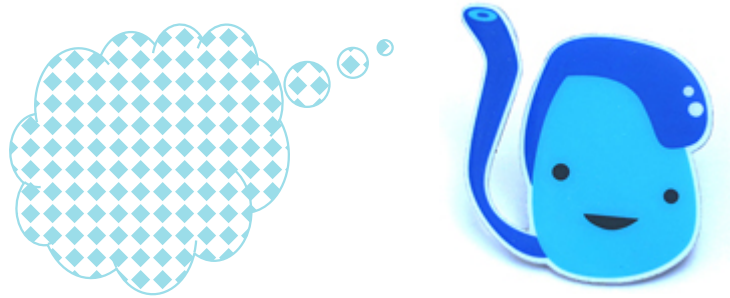
Primary Testicular Failure

↓ Testosterone
↓ Gonadotrophins

Hypogonadotrophic hypogonadism: due to hypothalamic-pituitary disease

↓ Testosterone
↑ Prolactin

Hyperprolactinaemi: rare



Semen Analysis:

Semen Analysis :-

Comment on:

- Volume
- Liquefaction time
- Sperm density (count)
- Motility
- The presence of abnormal spermatozoa (abnormal shape, or motility)
- pH
- WBCs

Testicular Failure:

- **Primary testicular failure:-**

* Damage to both the **interstitial cells and tubules** >> ↓ Testosterone & ↑ Gonadotrophins (LH & FSH)
* **Only tubular** impairment >> selective ↑ in FSH, while androgen may be Normal >> Because they are secreted from Interstitial cells of Lydig

HYPERPROLACTINAEMIA

Prolactin is an anterior pituitary hormone

Its secretion is tightly regulated:

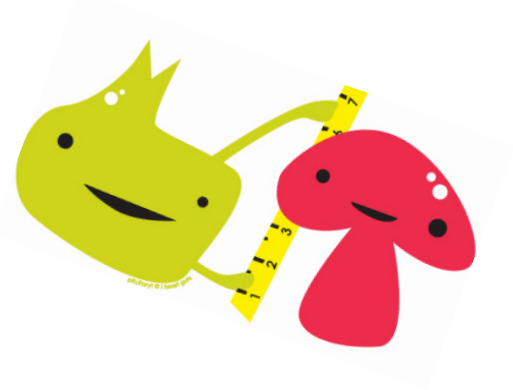
- **Stimulated by TRH** from the hypothalamus
- **Inhibited by dopamine** from hypothalamus

It acts directly on the mammary glands to control lactation

hyperprolactinaemia

- Hyperprolactinaemia is elevated circulating [Prolactin]
- A common condition
- It causes infertility in both sexes due to gonadal function impairment.
- **What is the early indication of hyperprolactinaemia?**
  - In women: amenorrhoea & galactorrhoea
  - In men: none

Causes of hyperprolactinaemia :-



- Stress
- Drugs. e.g. oestrogens, phenothiazines, metoclopramide, α-methyl dopa
- Seizures
- 1^{ary} hypothyroidism (prolactin is stimulated by the raised TRH)
- Other pituitary disease

If these are excluded..

- **Prolactinoma** (commonly microadenoma)
- Idiopathic hypersecretion (e.g. due to imparied secretion of dopamine that usually inhibits prolactin release)

Then these are the differential diagnosis..

Diagnosis of the cause of hyperprolactinaemia :-

Exclude:
- Stress
- Drugs
- Other disease

Differential diagnosis:
- prolactinoma or
- idiopathic hypersecretion

How to differentiate between prolactinoma & idiopathic hypersecretion?

1. Detailed pituitary imaging

2. **Dynamic tests of Prolactin secretion**: administration of TRH, then measure serum [prolactin]:
   - ➢ if elevated: idiopathic hyperprolactinaemia
   - ➢ If no rise: pituitary tumor

Summary

-Abnormal menstruation & infertility in women can arise from disease of the hypothalamus, pituitary, ovary, adrenal or thyroid
-In female, if there is a regular ovulating menstrual cycle, serum [progesterone] measured in the middle of the luteal phase (day 21) should be >30nmol/L
-If serum [progesterone] measured in the middle of the luteal phase (day 21) <10nmol/L: ovulation has not occurred
-Endocrine causes of infertility in the male are rare
-In both male and female Infertility, a serum [FSH] >25U/L indicates 1ary gonadal failure
-Hyperprolactinaemia is a rare cause of male infertility
-Prolactin is stimulated by TRH and inhibited by dopamine from hypothalamus
-Prolactinoma and Idiopathic prolactin hypersecretion are the final differential diagnoses for hyperprolactinaemia when all other causes are excluded.

Test your knowledge ..!

1- As an endocrine investigation we should measure which one of the following to confirm presence of ovulation :

A) FSH
B) LH
C) Progesterone
D) Estrogen

2- A 30-year-old woman comes to clinic to discuss abnormal menstrual periods. Menarche was at age 14. Her periods were never entirely predictable but over the past year they have been occurring less often, about every two or three months. Her last menstrual period was two months ago. She has not been sexually active for over a year. She has no chronic medical problems. After the investigation done ,, the doctor told her that she had a condition called PCOS. (Polycystic ovarian syndrome) From the following which one of the hormones profiles is identical for her :

A) Low level LH , high level FSH
B) High level LH , high level FSH
C) Low level LH , low level FSH
D) High level LH, low level FSH

1.C
2.D

آخر محاضرة

الشكر لله أولاً

ومن ثم لجميع الأعضاء والعضوات الذين بذلوا أوقاتهم وجهودهم في سبيل انجاح التيم

نتمنى أن نكون قد أفدناكم طوال العامين

وعذراً على أي تقصير =(

Biochemistry Team Leaders 432

If you find any mistake, please contact us:)

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Thank you