OVULATION DISORDERS

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AGENDA

- BACKGROUND
- CLASSIFICATIONS OF OVULATION DISORDERS
- TNE ELABORATION OF THE 2022 FIGO CLASSIFICATION OF ANOVULATION
- MANAGEMENT

BACKGROUND

- Ovulation disorder (OD) is a term that describes a group of disorders in which ovulation fails to occur , occurs on an infrequent or irregular basis. Ovulatory disorders are one of the leading causes of infertility.

- Ovulatory disorders are common causes of *amenorrhea*, *AUB-O*, and *infertility*, and are frequent manifestations of *polycystic ovary syndrome (PCOS).*

BACKGROUND

- Ovulatory disorders are common in girls and women of reproductive age and are associated with *episodic or chronic dysfunction of the hypothalamic–pituitary–ovarian (H-P-O) axis*.
- Ovulatory disorders are often associated with underlying endocrinopathies, neoplasms, psychological and psychiatric conditions, and the use of specific pharmacologic agents.
- These disorders may *adversely affect quality of life* when they manifest with infertility or as aberrations in menstrual function ranging from *AUB to amenorrhea*.

CLASSIFICATION OF OVULATORY DISORDERS

- Many classification systems have been introduced since 1973 , however, non of them was perfect. Those classifications included the following:

1. **The original WHO classification** presented 3 types of ovulatory dysfunction (1973).
2. **A second WHO classification 1976** presented 7 types of ovulatory dysfunction depending on

   a-PRL was elevated or normal ,

   b-Response to a progestogen challenge test to assess estrogenisation

   c-FSH concentration was elevated or normal

3. **NICE GUIDELINES (2004)** describing 3 groups depending on both gonadotropin and estradiol levels.
4. **FIGO CLASSIFICATION (2022) OVULATION DYSFUNCTION (SEE LATER).**

CLASSIFICATION OF OVULATORY DISORDERS

The previous classifications *(from 1-3 previous slide)* has the following limitations:

1-Anovulation is only one extreme of ovulatory dysfunction that includes a spectrum of manifestations that range from isolated episodes to chronic ovulatory failure.

2-Hormone levels do not obey clear rules. E. g. hypothalamic amenorrhea who are underweight, LH levels are usually suppressed, while FSH levels are often in the normal range.

3-Women with ***PCOS*** often have levels of FSH & LH in the normal range.

(Morrison AE, 2021)

CLASSIFICATION OF OVULATORY DISORDERS

- ***The FIGO ovulatory disorders classification system is the culmination of a rigorous and inclusive process directed by two of FIGO's committees and involving experts, national and subspecialty societies and journals, as well as patient advocacy groups from six continents.***
- *This work demonstrates FIGO's ability to assemble and lead an inclusive network of stakeholders to deal with a global health care issue in a fashion that should address an important unmet need.*

FIGO
International Federation of Gynecology and Obstetrics
the Global Voice for Women's Health

CLASSIFICATION OF OVULATORY DISORDERS

"The FIGO ovulatory disorders classification system should facilitate education, clinical care, and the design and interpretation of basic, translational, clinical and epidemiological research in a way that **improves care for the hundreds of millions of women affected by ovulatory disorders worldwide."**

– Professor Malcolm Munro, Past Chair,
FIGO Committee on Menstrual Disorders and Related Health Impacts

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CLASSIFICATION OF OVULATORY DISORDERS

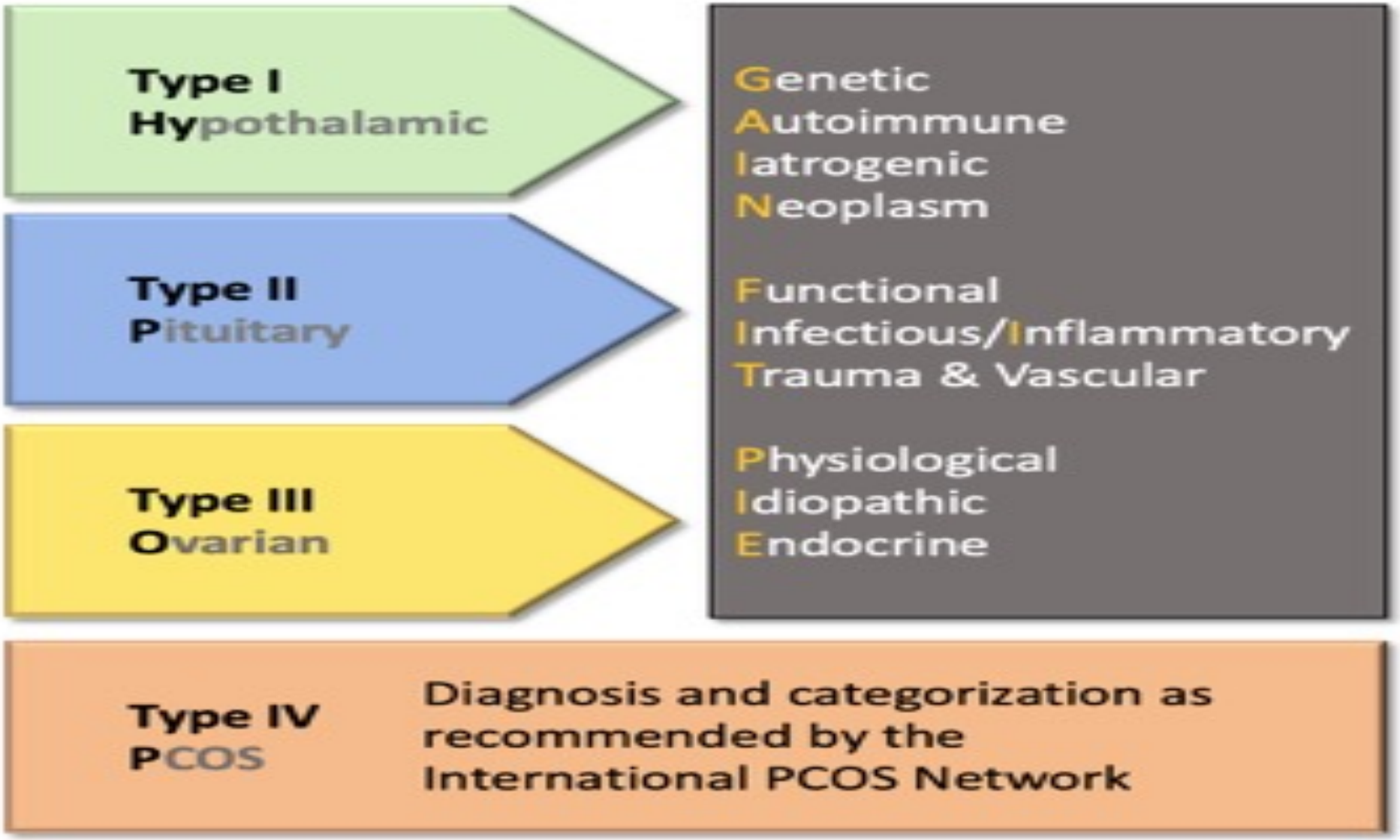
- The new system recognizes 3 basic strata once an ovulatory disorder has been diagnosed. *The 1st level* is categorization by *one of the four* primary categories as follows:

Type I: Hypothalamus; Type II: Pituitary;

Type III: Ovary; and Type IV: PCOS.

- *The second level* requires assignment to the known or suspected anatomically based abnormality as directed by the GAIN-FIT-PIE acronym.
- *The third or tertiary level* identifies a specific entity causing or contributing to the ovulatory disorder.

FIGO Ovulatory Disorders Classification (HyPO-P)



Categorization in the FIGO Ovulatory Disorders Classification System

- Categorizing into these levels requires that *the clinician perform whatever investigations deemed appropriate to localize the site and the presumed underlying mechanism contributing to ovulatory dysfunction*.
- For example, the individual with infrequent and irregular menses, galactorrhea, elevated prolactin, and a magnetic resonance image demonstrating a pituitary tumor would categorize as a **type 2 – N (pituitary neoplasm).**

Categorization in the FIGO Ovulatory Disorders Classification System

- Another example ; a woman with irregular and infrequent menstruation, mild hirsutism, and sonographic evidence of at least one symmetrically enlarged ovary (≥10 ml) or an ovary with more than 20 follicles without a dominant follicle or corpus luteum, a circumstance that dictates a **type 4 – PCOS** classification.

Categorization in the FIGO Ovulatory Disorders Classification System

It is recognized that the precision in determining the anatomic location and the mechanism of pathogenesis is somewhat aspirational and will vary to a degree by the disorder and the resources available to the clinician.

MANAGEMENT ACCORDING TO GONADOTROPIN & PROLACTIN LEVELS

1. ANOVULATION WITH ABNORMALLY LOW GONADOTROPINS [WHO -I]: HYPOGONADOTROPIC
2. ANOVULATIO WITH ABNORMALY HIGH GONADOTROPINS [WHO-II]: HYPERGONADOTROPIC
3. ANOVULATION WITH NORMAL GONADOTROPINS [WHO-III]: EUGONADOTROPIC
4. ANOVULATION WITH ELEVATED PROLACTIN [WHO-IV]: HYPERPROLACTINEMIA

ANOVULATION WITH ABNORMALLY LOW GONADOTROPINS [HYPOGONADOTROPIC]

HYPOTHALAMIC CAUSES	PITUITARY CAUSES
1- Dysfunction (Anorexia N, Stress, severe exercise) 2. Congenital (Kallaman's syndrome) 3. Organic lesions (Trauma, inflammation, tumors)	1- Congenital syndromes 2-Sheehan's syndrome 3.Trauma (surgery, irradiation) 3. Inflammation 5. Tumors (craniopharyngioma)

ANOVULATION WITH ABNORMALLY LOW GONADOTROPINS [HYPOGONADOTROPIC] TREATMENT

Induction of ovulation with either GnRH (in hypothalamic problems) or gonadtrophins (in pituitary problems)

- **GnRH therapy:** GnRH should be given in a pulsatile manner

- **Gonadotrphin therapy**
  - Combined FSH (75 IU) and LH (75 IU)
  - FSH alone
  - LH alone (or hCG)

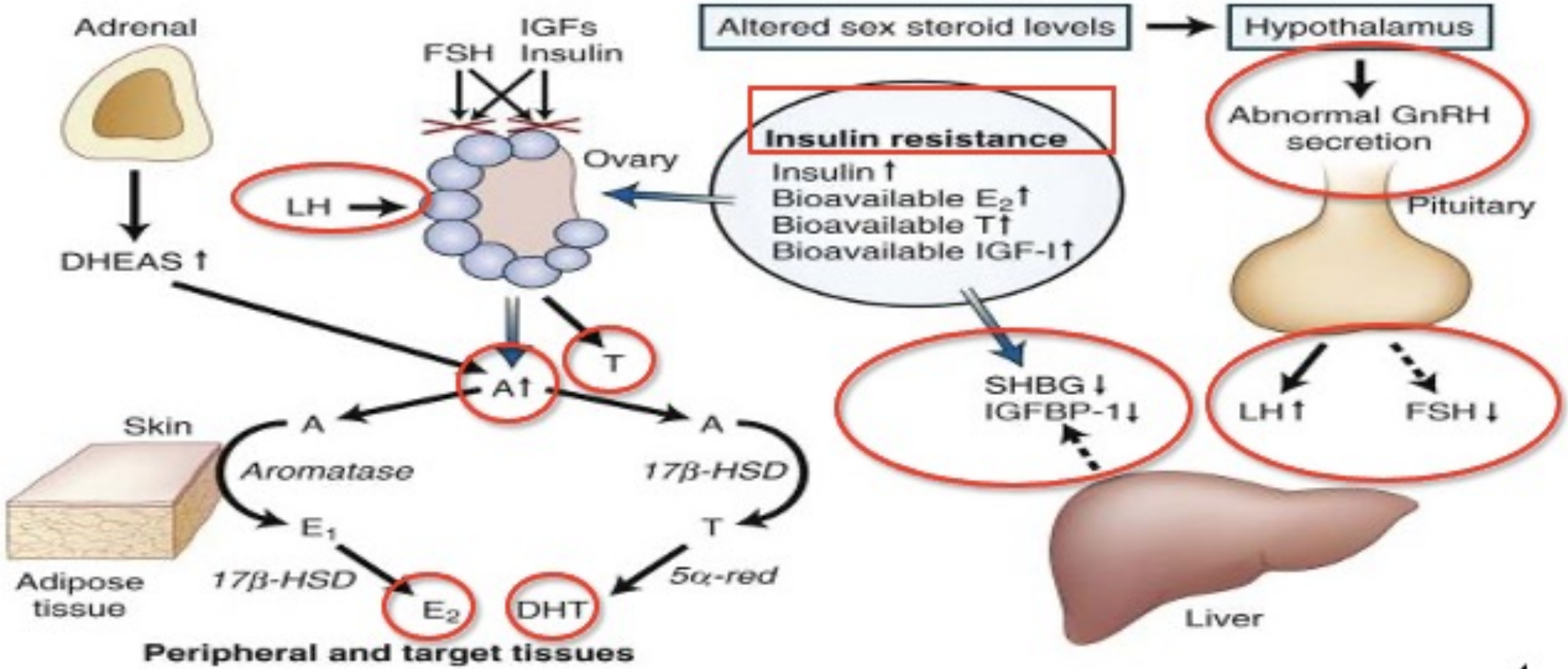
ANOVULATION WITH ABNORMALLY HIGH GONADOTROPINS [HYPERGONADOTROPIC]

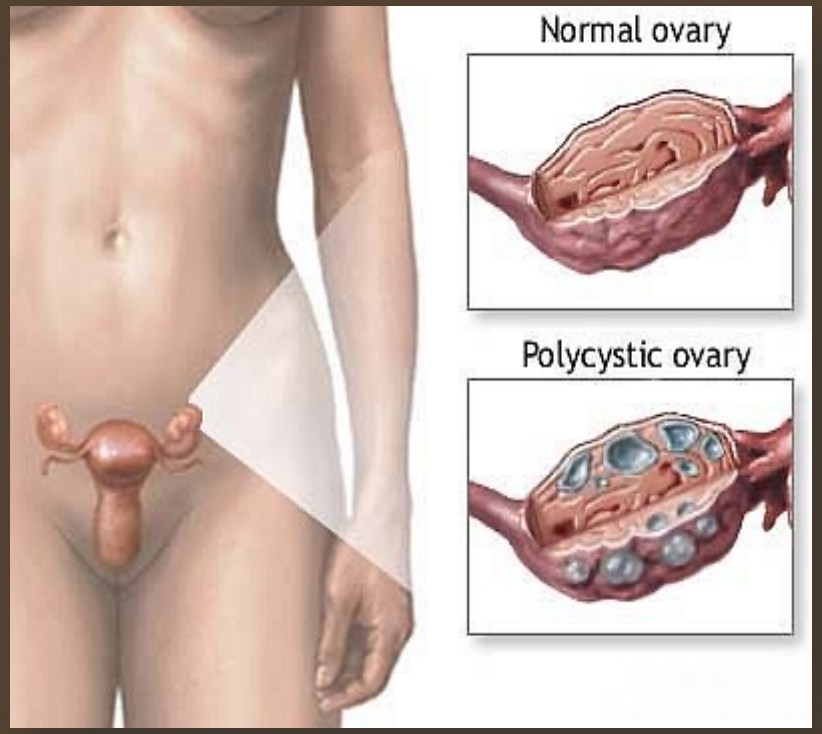
CAUSES	TREATMENT
1-Streak gonads e.g Turner's syndrome 2-Resistant ovary syndrome 3-Premature ovarian failure: ***-Spontaneous*** ***-Trauma i.e surgery*** ***-Chronic inflammation*** ***-Irradiation, Chemotherapy***	• **NO current treatment** • **Oocyte donation** • **Stem cell therapy??**

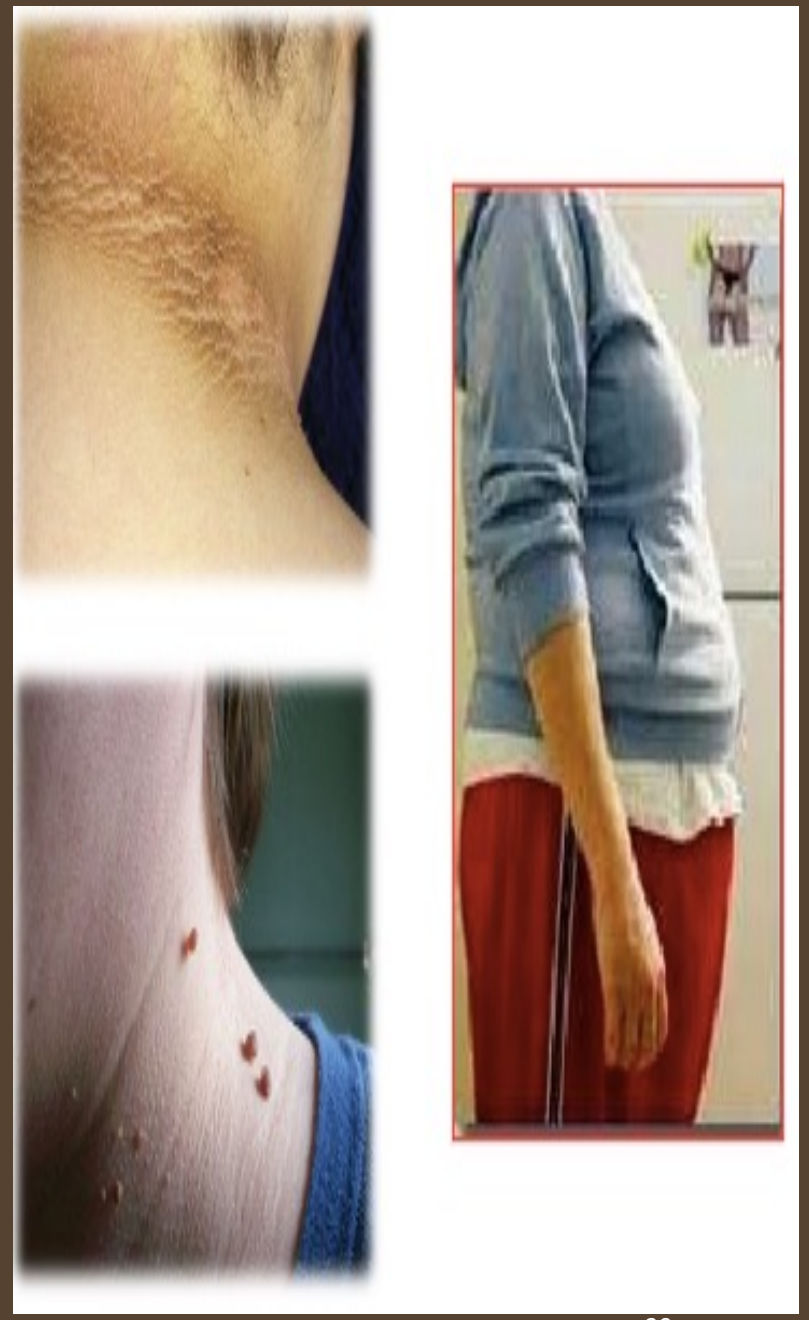
ANOVULATION WITH NORMAL GONADOTROPINS [EUGONADOTROPIC]

- The so-called normo-gonadotropic, normo-estrogenic cases, which constitute by far the largest group of patients is more problematic than other groups.
- This group is a mixture of different hormonal dysfunctions which can primarily originate from diverse glandular and even extra-glandular sources.
- The most notorious subgroup among them is made up of patients with the PCO syndrome (PCOS), which is an amalgam of different pathophysiological mechanisms.

PCOS - Pathophysiology




Normal ovary
Polycystic ovary



ANOVULATION WITH ELEVATED PROLACTIN : HYPERPROLACTINEMIA

PHYSIOLOGICAL CAUSES	PATHOLOGICAL CAUSES
1. Pregnancy 2. Lactation 3. Sexual excitement 4. Stress	1. Pituitary adenomas (micro/macro) 2. Primary hypothyroidism 3. Drugs (reserpine, psychotic drugs, OCPs, H2 blockers..) 4. Chronic renal failure 5. Chest wall injuries, surgeries or HZI

ANOVULATION WITH ELEVATED PROLACTIN : HYPERPROLACTINEMIA

CLINICAL DIAGNOSIS	INVESTIGATIONS
1. Galactorrhea 2. Oligo/amenorrhea 3. Abnormal uterine bleeding 4. Infertility 5. PMS 6. Sexual dysfunction	1. Serum prolactin >20ng/ml 2. MRI pituitary (to exclude adenomas >100ng/ml) 3. Serum TSH 4. Review therapeutic history

TREATMENT BY : Surgical removal of macroadenoma, or medications as bromocriptine and cabergolin

THANK YOU FOR ATTENSION