ROLE OF HORMONAL ASSAY IN DIAGNOSING PCOD

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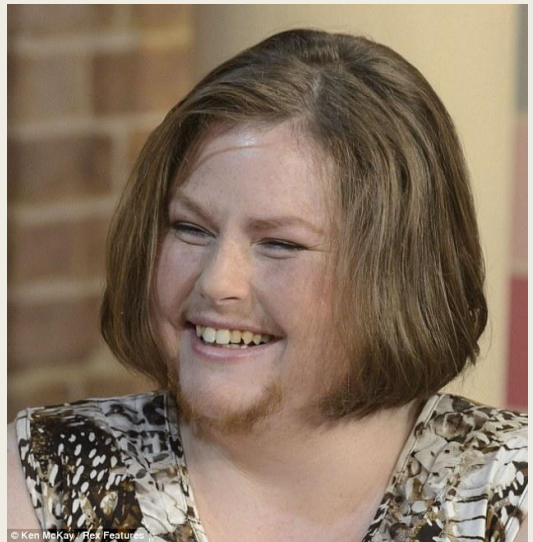
- In 1935, **Stein and Leventhal** described 7 women with bilateral enlarged PCO, amenorrhea or irregular menses, infertility and masculinizing features.

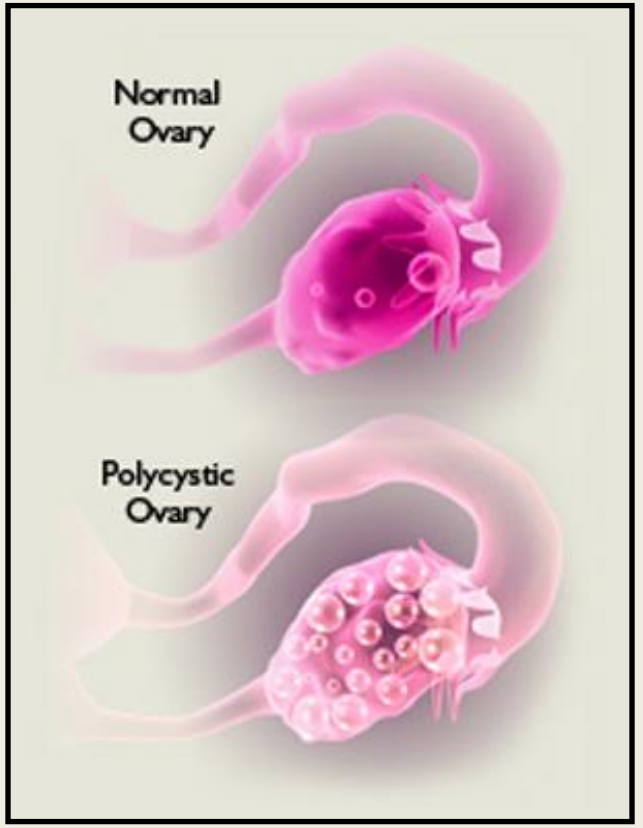
- This paper introduced clinicians to the concept of reproductive endocrinopathies



- PCOS is a complex endocrine disorder affecting women of child bearing age characterised by increased androgen production and ovulatory dysfunction.

- It is the **most common endocrine** disorder of **reproductive-aged women** and affects approximately 5 to 10 %.(Norman et all 2007)

- PCOS is the leading cause of anovulatory infertility and hirsutism
- **20-33% of all reproductive age group have polycystic ovaries**
- 5-10% of all reproductive age group have PCOS
- 87% of women have oligomenorrhoea
- 26% of them have amenorrhoea
- **50% of them present with infertility**
- 50% of women with recurrent miscarriages



Laboratory Investigations

No consensus regarding specific lab test for PCOS

- To document hyperandrogenism.
- To rule out other endocrinopathies.
- Look for metabolic abnormalities (commonly seen with PCOS).

The underlying defects in PCOS are still unclear, however insulin resistance and metabolic syndrome are common in both obese and non-obese PCOS patients, so that evaluation of glucose tolerance is recommended.

Following hormone levels are measured when considering a PCOS diagnosis

- LH
- FSH
- TOTAL AND FREE TESTOSTERONE
- DEHYDROEPIANDROSTERONE SULFATE (DHEA S)
- PROLACTIN
- ANDROSTEINDIONE
- PROGESTERONE
- ESTROGEN

OTHERS:

TSH

LIPID PROFILE

FASTING INSULIN

OGTT

LH AND FSH:

- These hormones secreted by the pituitary gland
- At the beginning of the cycle **LH and FSH levels** range between **5-20 miu/ml.**
- Most women have equal amounts of LH and FSH during early part of their cycle
- However there is **LH surge** before ovulation , LH increases to about **25-40** miu/ml
- While many women with pcos still have FSH 5-20 miu/ml , their LH level is often 2 or 3 times that of FSH (elevated LH to FSH ratio)
- An **increased** ratio of **LH to FSH of >2** is found in **60% to 70% of women with PCOS** and is more commonly seen in non-obese women.
- This change in the LH , FSH ratio is enough to disrupt ovulation
- **While this used to be considered important in diagnosing PCOS it is now considered less useful**

TESTING FOR **HYPERANDROGENEMIA**

- Done by testosterone levels
- Total testosterone & Free testosterone
- single most sensitive test for the detection of androgen excess.
- **Normal** upper limit for serum total testosterone in adult women is approximately **40 to 60 ng/dL (1.4 to 2.1nmol/L)**
- Women with pcos have an increased levels of both total and free testosterone
- A slight increase in testosterone can suppress normal menstruation and ovulation.

- **Dehydroepiandrosterone sulfate (DHEAS) –marker** for **adrenal hyperandrogenism**
- Used to detect adrenal tumor
- It is normal for women to have DHEA s level anywhere between 35-430 mcg/dl
- **Most women with PCOS have DHEAS level greater than 200mcg/dl.**
- Adrenal tumor → DHEAS levels are often markedly elevated (>700 mcg/dL, 13.6 mmol/L)

PROLACTIN :

- prolactin levels are ususally normal in women with pcos generally < 25 ng/ml .
- It is important to check for high prolactin levels in order to rule out pituitary tumors that might be causing PCOS symptoms.
- Some women with PCOS have (5-30%) have elevated prolactin levels falling within 25-40 ng/ml.

ANDROSTENEDIONE:

- Androstenedione is an hormone produced by the ovaries and adrenal galnds
- Sometimes high levels can affect estrogen and testosterone levels
- Normal range- 0.7-3.1 ng/ml

Progesterone:

- For women with PCOS especially those on fertility treatment , progesterone levels are checked about 7 days after it is thought that ovulation has occurred.
- If progesterone levels are high (> 14 ng/ml) this means ovulation has occurred .
- This test is important because sometimes women with pCOS have some signs that ovulation is occurring , however when progesterone tests is done it shows that ovulation did not occur.

Estrogen :

- Most women with PCOS have their estrogen levels within normal range (25-75 pg/ml). This is due to high levels of insulin and testosterone found in women with pcos are converted to estrogen.

TSH:

- Women with pcos have normal TSH.
- TSH done to rule out thyroid disesase which cause menstrual irregularities.

INSULIN AND GLUCOSE:

- PCOS caused by insulin resistance . Women should have FBS and GTT at diagnosis
- Raised fasting insulin >25 micro iu/ml and fasting glucose/insulin ratio <4.5 suggests insulin resistance.
- Serum insulin levels > 300 after 2 hr 75 glucose load suggests severe IR.

CONCLUSION

- The Royal College of Obstetricians and Gynaecologists (RCOG) **recommends (NOT GUIDELINES!!)**the following baseline screening tests for women with suspected polycystic ovarian syndrome (PCOS):
- Thyroid function tests
- serum prolactin levels
- Free androgen index (defined as total testosterone divided by sex hormone binding globulin [SHBG] × 100, to give a calculated free testosterone level).

CONCLUSION

- LH andFSH measurements have sensitivity of only 35% and 41-44%, respectively.
- **Mean serum total testosterone concentration was the most frequent abnormal biochemical marker for PCOS with sensitivity of 70%.**
- Testosterone, androstenedione and LH in combination, increased sensitivity to 86%.
- Using LH/FSH ratio as a biochemical criterion for diagnosis of PCOS should be abandoned because of its low sensitivity.
- To be of value the **normal range** for all hormones should be precisely defined in a group of regularly ovulating women in the early follicular phase of the cycle for the assay used in each laboratory.

CONCLUSION

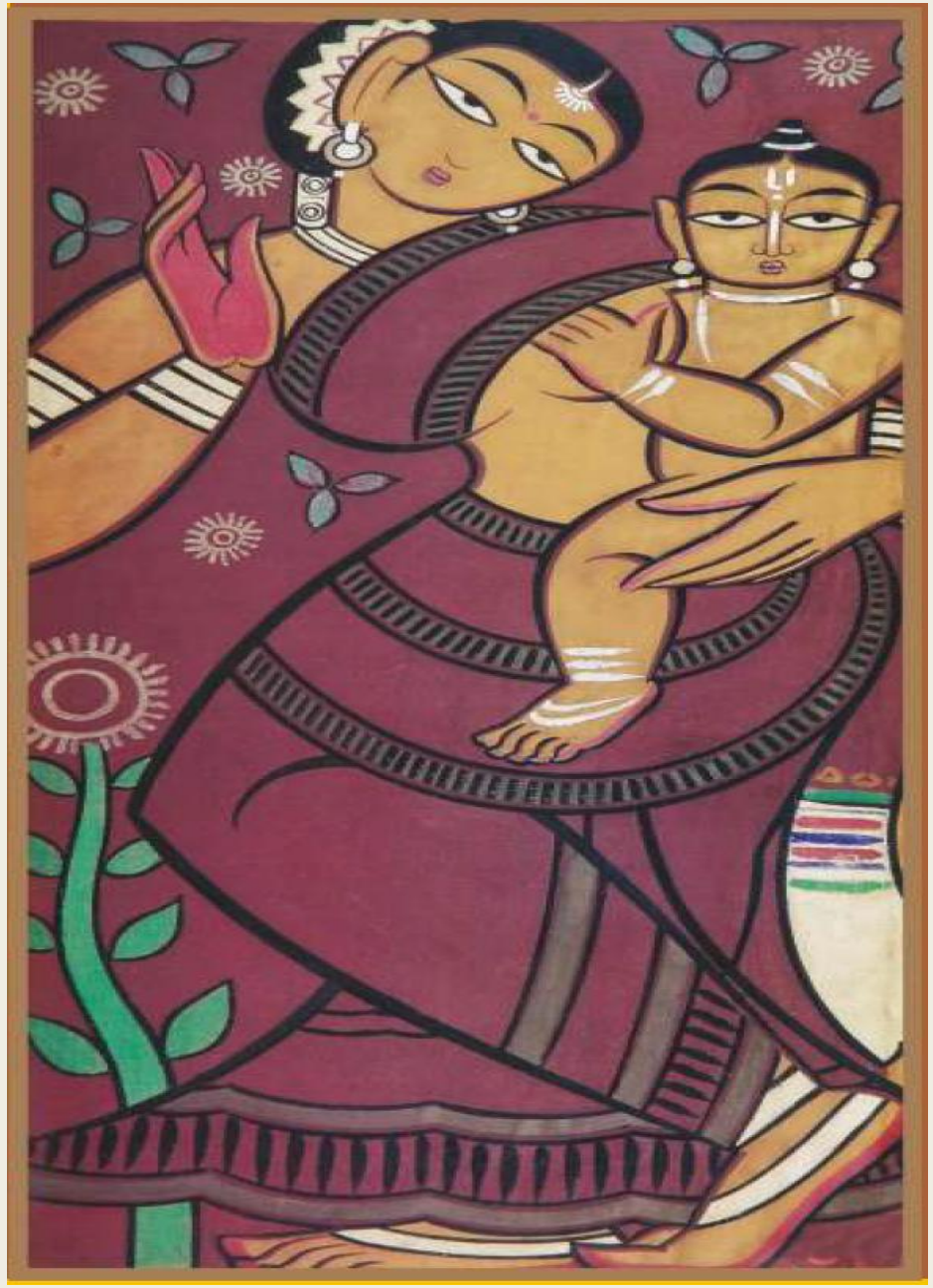
- It is important to remember that with all women, hormone levels can very greatly.
- It is also important to mention that since the “normal” ranges vary greatly for some hormones (especially since each lab sets its own “normal” values for these hormones),
- Also some women with PCOS have hormone levels that appear within the “normal” range, but still suffer from symptoms and still might have PCOS.
- **Unfortunately, many physicians are not familiar enough with PCOS to understand that even small changes in hormone levels can cause PCOS-related symptoms.**

ON GOING RESEARCH

- Elevated Serum Level of Anti-Mullerian Hormone in Patients with Polycystic Ovary Syndrome has direct Relationship to the Ovarian Follicle Excess and to the Follicular Arrest

(Journal of clinical endocrinology JCEM ;2013)

- A New Contributing Factor to Polycystic Ovary Syndrome: The Genetic Variant of Luteinizing Hormone



THANK YOU

JCEM-AMH

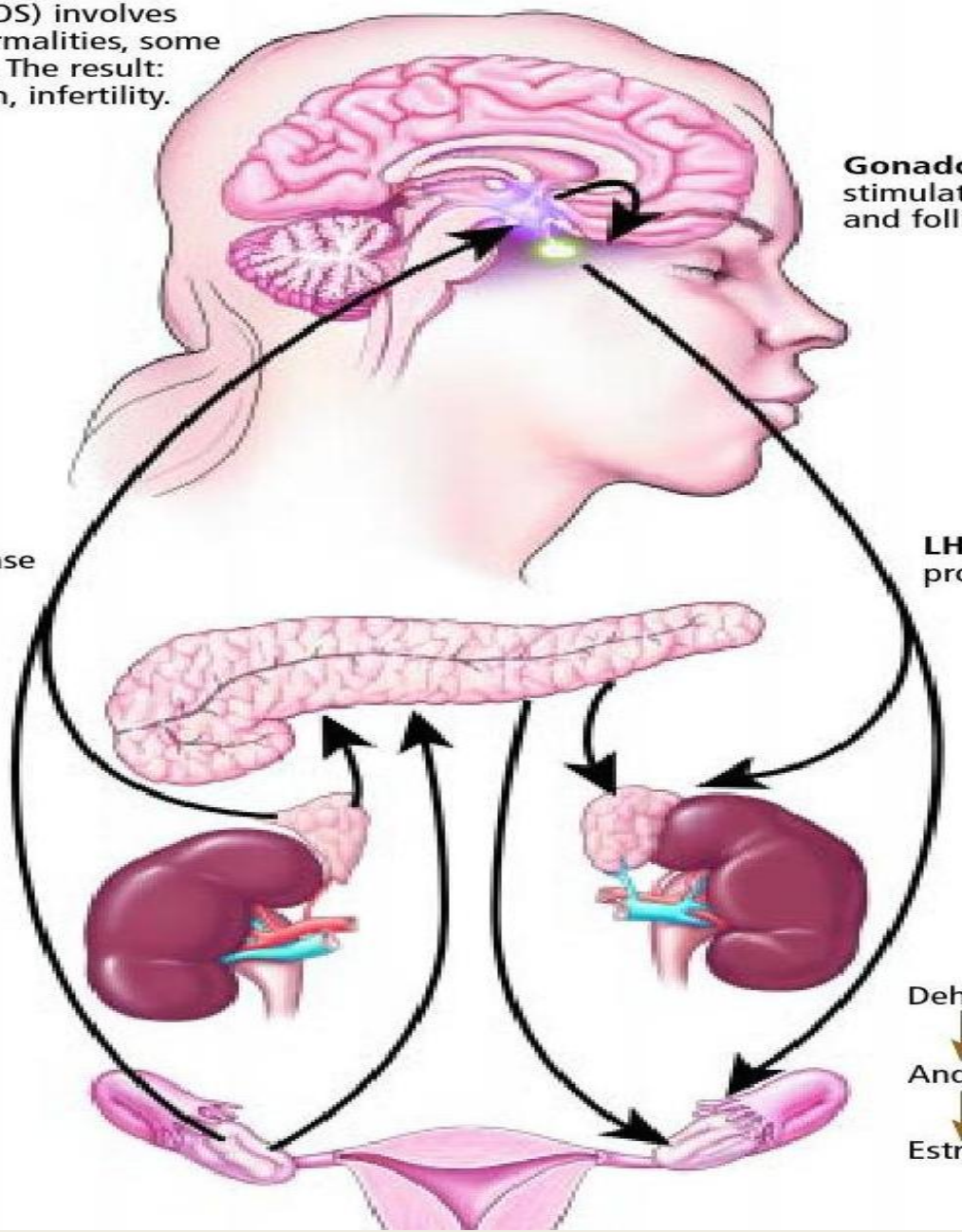
- In the ovary, AMH is produced by the GC from preantral and small antral follicles .
- From experimental data, mainly obtained in rodents, the proposed functions of AMH are 1) inhibition of the initial recruitment of primordial follicles, through a paracrine effect
- 2) inhibition of aromatase activity in GC, thus reducing the production of estradiol (E2) .
- This last effect combined with the fact that AMH could reduce the follicle sensitivity to FSH in the mouse both *in vitro* and *in vivo* raises the possibility that an excessive production of AMH could be involved in the follicular arrest of PCOS

Jcem v-LH

- The high overall frequency of the v-LH_β allele in women in general and its low frequency in obese PCOS patients suggest that v-LH has a role in reproductive functions and may somehow contribute to the pathogenesis of PCOS in obese individuals.
- Although it remains unknown whether the two mutations in v-LH_β lead to a net increase or decrease in the overall LH action
- it is tempting to speculate that it offers advantage or disadvantage to certain individuals depending on their genetic background and environment.
- Hyperinsulinemia, hyperandrogenism, and dyslipidemia are commonly found in women with PCOS (16, 17).
- **PCOS appears often at a young age, and therefore, we should be able to identify young women at future risk of these hormonal and metabolic changes. As a prognostic or diagnostic approach, the detection of v-LH may allow the discrimination between individuals with high and low risks of PCOS.**

What causes polycystic ovary syndrome?

Although the inciting event is not known, polycystic ovary syndrome (PCOS) involves interactions of hormonal abnormalities, some of which are self-perpetuating. The result: hyperandrogenism, anovulation, infertility.



Gonadotropin-releasing hormone (GnRH) stimulates release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH)

Estrone controls LH release

LH is increased, stimulating androgen production

Insulin promotes hyperandrogenism (and perhaps vice versa)

Follicle-stimulating hormone (FSH) may be low, inhibiting production of estradiol in favor of testosterone and estrone

Dehydroepiandrosterone sulfate (DHEA-S)
↓
Androstenedione → Testosterone
↓
Estrone

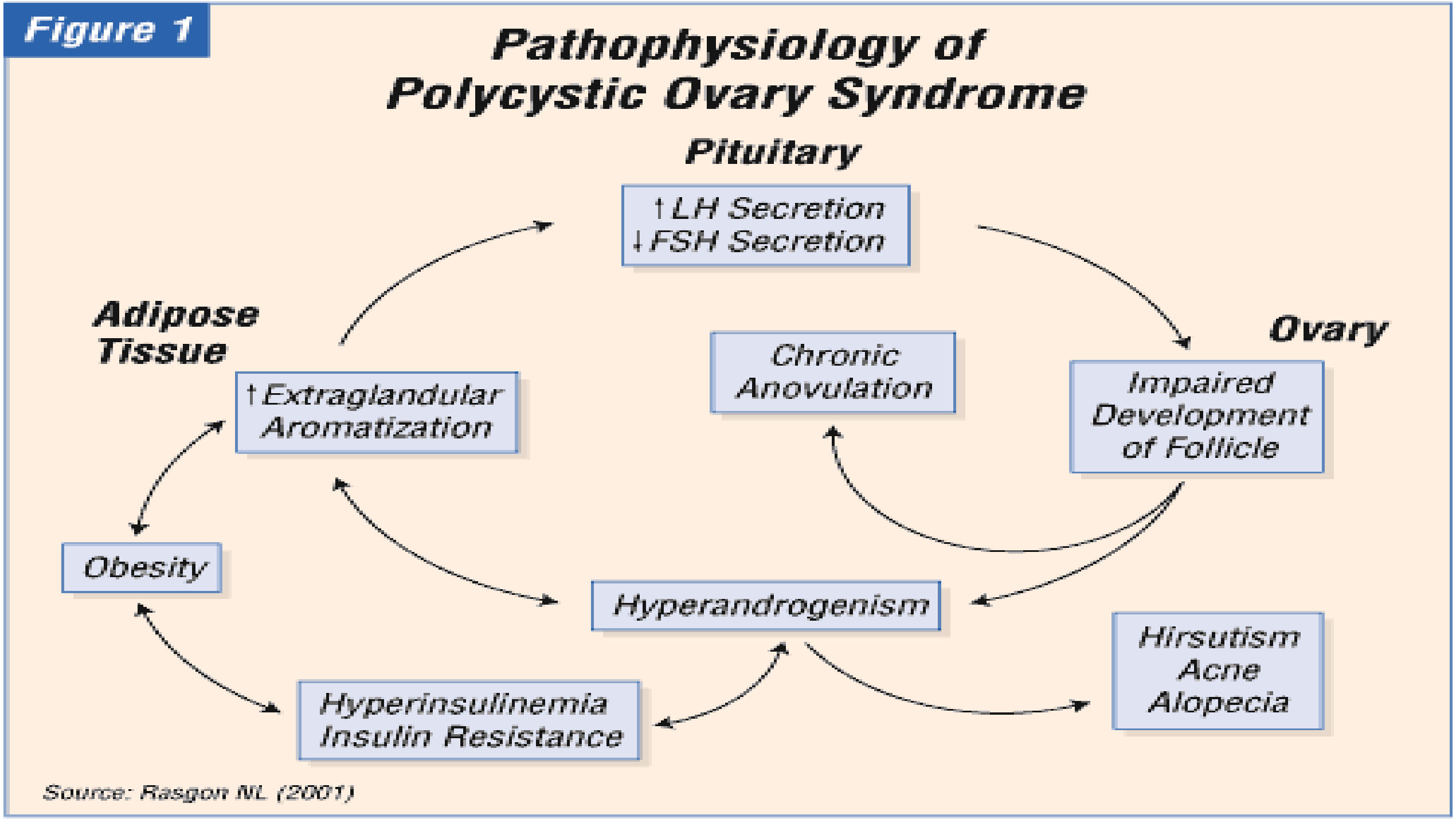
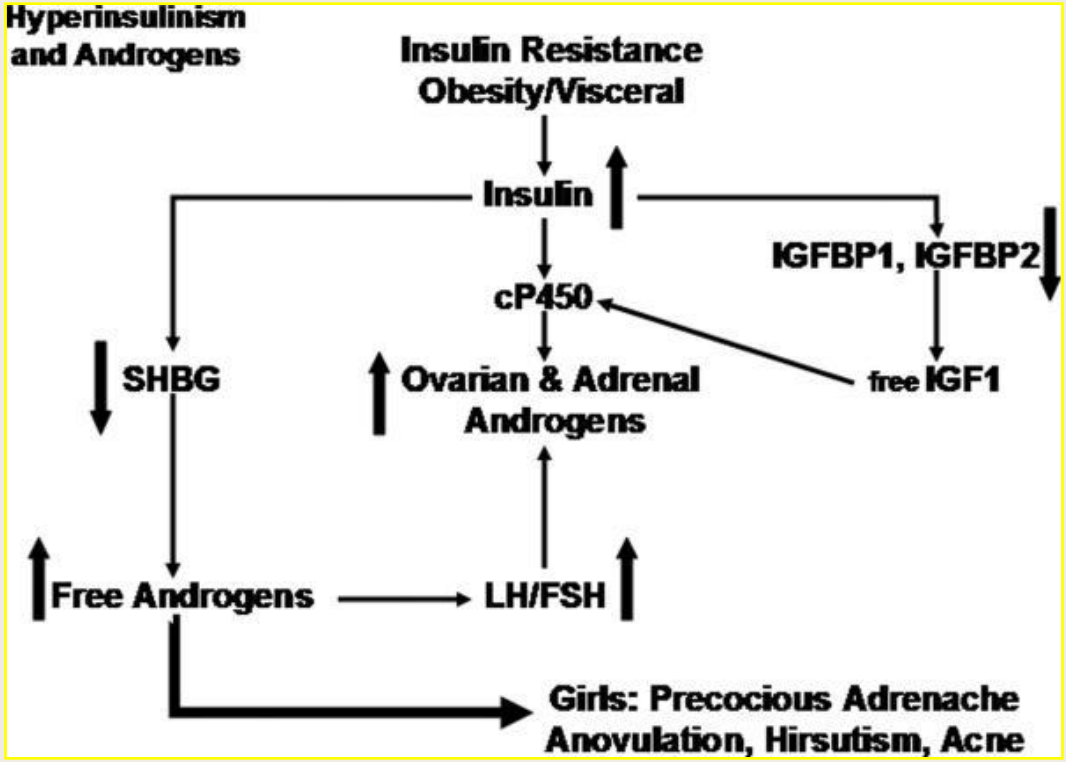


Figure 1
Pathophysiology of Polycystic Ovary Syndrome
Pituitary
↑ LH Secretion
↓ FSH Secretion
Adipose Tissue
Ovary
↑ Extraglandular Aromatization
Chronic Anovulation
Impaired Development of Follicle
Obesity
Hyperandrogenism
Hyperinsulinemia Insulin Resistance
Hirsutism Acne Alopecia
Source: Rasgon NL (2001)

The Role of Insulin Resistance/ Hyperinsulinemia in Hyperandrogenism

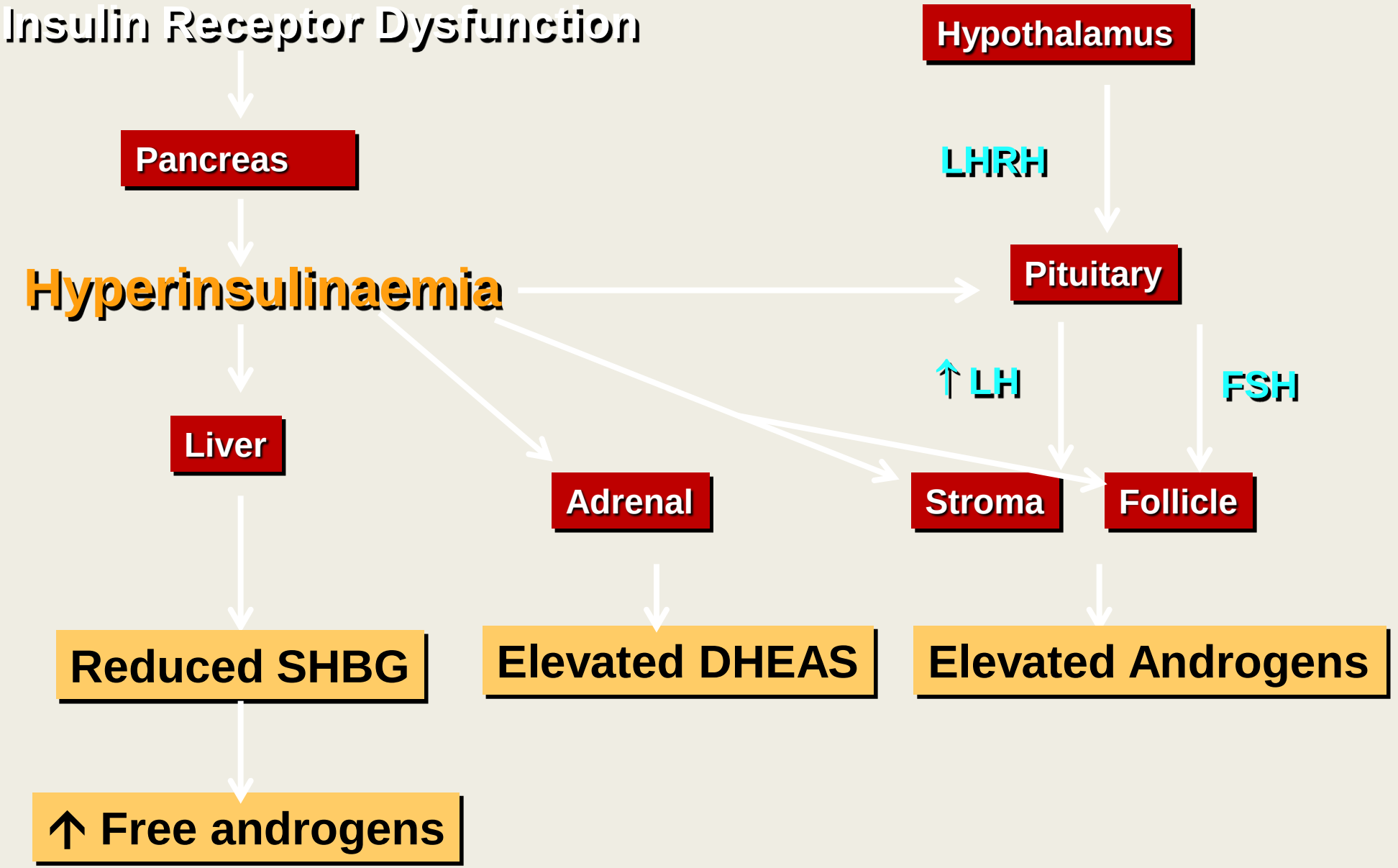


- Diagnostic criteria for insulin resistance syndrome in women

Any 3 or more of the following

- Waist circumference > 88 cm
- Triglycerides >150mg/dl
- HDL <50MG/DL
- FBS> 100MG/DL
- BP >130/85 mmhg

Hyperinsulinaemia & Hyperandrogenaemia



Differential diagnosis

1. Virilizing congenital adrenal hyperplasia
2. Cushing's syndrome
3. Virilizing tumors
4. Hyperprolactinemia
5. Insulin-resistance disorders
6. Acromegaly
7. Thyroid dysfunction
8. Drugs