Polycystic Ovary Syndrome

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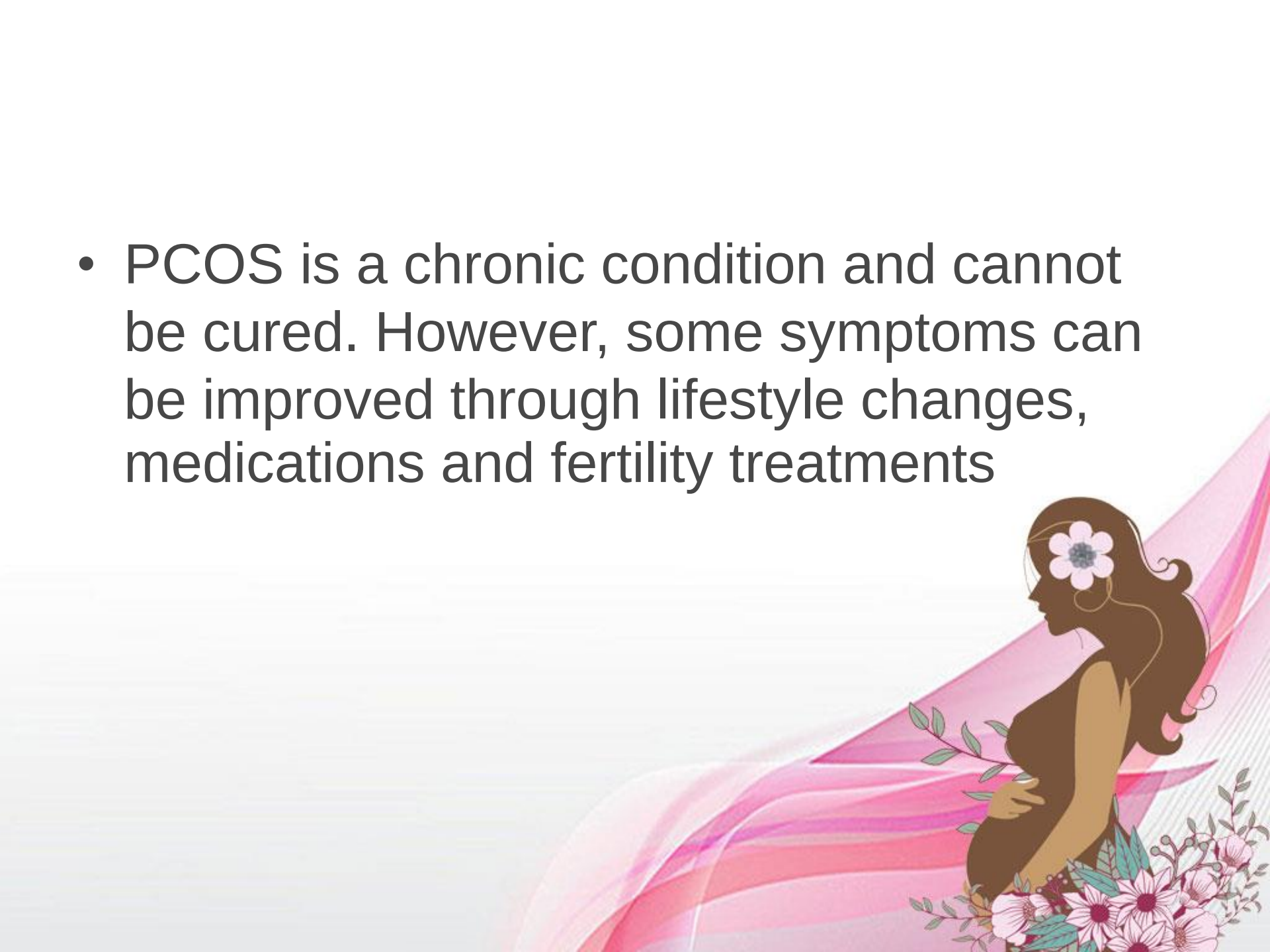
Introduction

- Polycystic ovarian syndrome(PCOS) is a common reproductive endocrinopathy that impacts many aspects of a women health and fertility potential

- PCOS is a chronic condition and cannot be cured. However, some symptoms can be improved through lifestyle changes, medications and fertility treatments



Definition: PCOS is a syndrome of ovarian dysfunction along with the cardinal features of hyperandrogenism and polycystic ovary morphology

Prevalence: PCOS is the most common endocrine disorder in women, it affects around 5-10% of women of reproductive age. The prevalence of PCO seen on U/S is much higher-around 25%.

Aetiology

- Women with the syndrome have an increased ovarian cytochrome P450 activity & partly to increased LH stimulation.

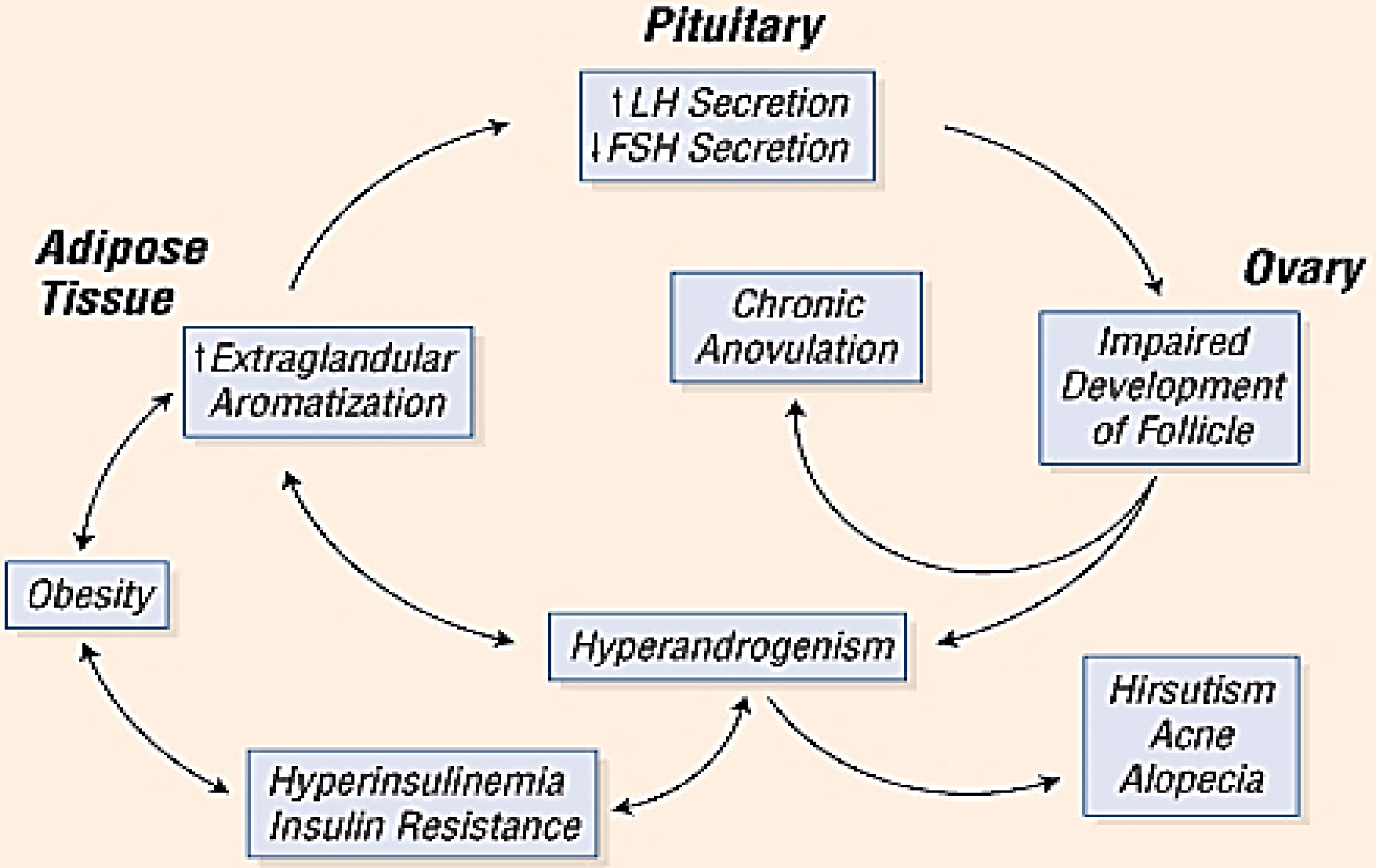
- The role for peripheral insulin resistance with the resulting hyperinsulinemia also promoting ovarian androgen production.

- Recent studies looking at the role of a complex interaction between obesity & reproductive function in the etiology of PCOS mediated by ghrelin. Ghrelin is a gastric peptide which has adipogenic properties. Ghrelin levels were found to be lower in obese women with PCOS.

- Studies on genetics of PCOS do suggest that a gene or several genes may be associated with PCOS. PCOS appear clustering in families.

Figure 1

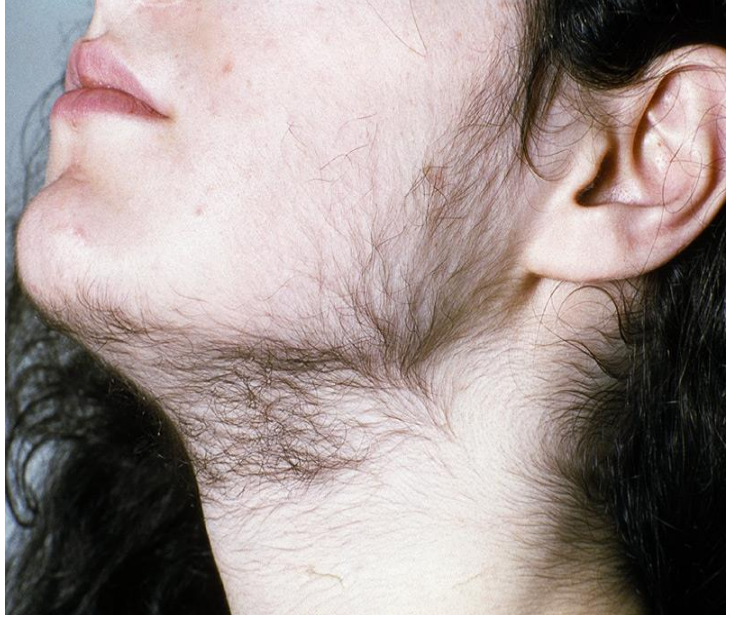
Pathophysiology of Polycystic Ovary Syndrome

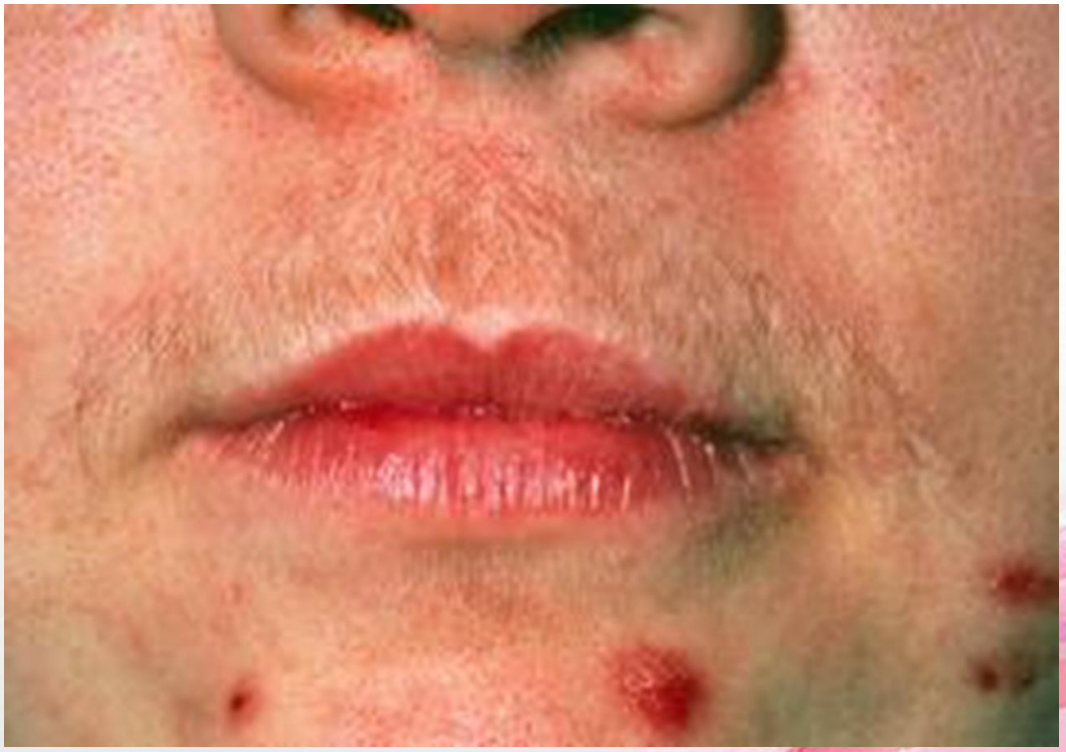


Source: Rasgon NL (2001)

Clinical Features

- **Oligomenorrhoea/amenorrhea**: This occurs in up to 65-75% of PCOS patients & is predominantly related to chronic anovulation.
- **Hirsutism**: Occur in 30-70% of women.
- **Subfertility**: In up to 75%.
- **Obesity**: 40% are clinically obese.
- **Recurrent miscarriage**: Seen in 50-60% of women with more than 3 early pregnancy losses.
- **Acanthosis nigricans**: Occur in around 2% of women with PCOS. Are areas of increased skin pigmentations that are velvety in texture seen in axilla & other flexures.
- **Others**: Acne & female androgenic alopecia.
- **Asymptomatic**: With polycystic ovaries on ultrasound.





PCOS SYMPTOMS

HAIR LOSS

HIRSUTISM

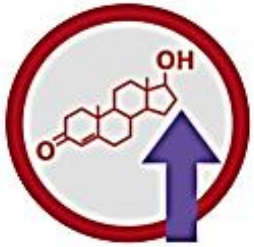
PELVIC PAIN

INFERTILITY

OVERWEIGHT

IRREGULAR PERIODS

FATIGUE



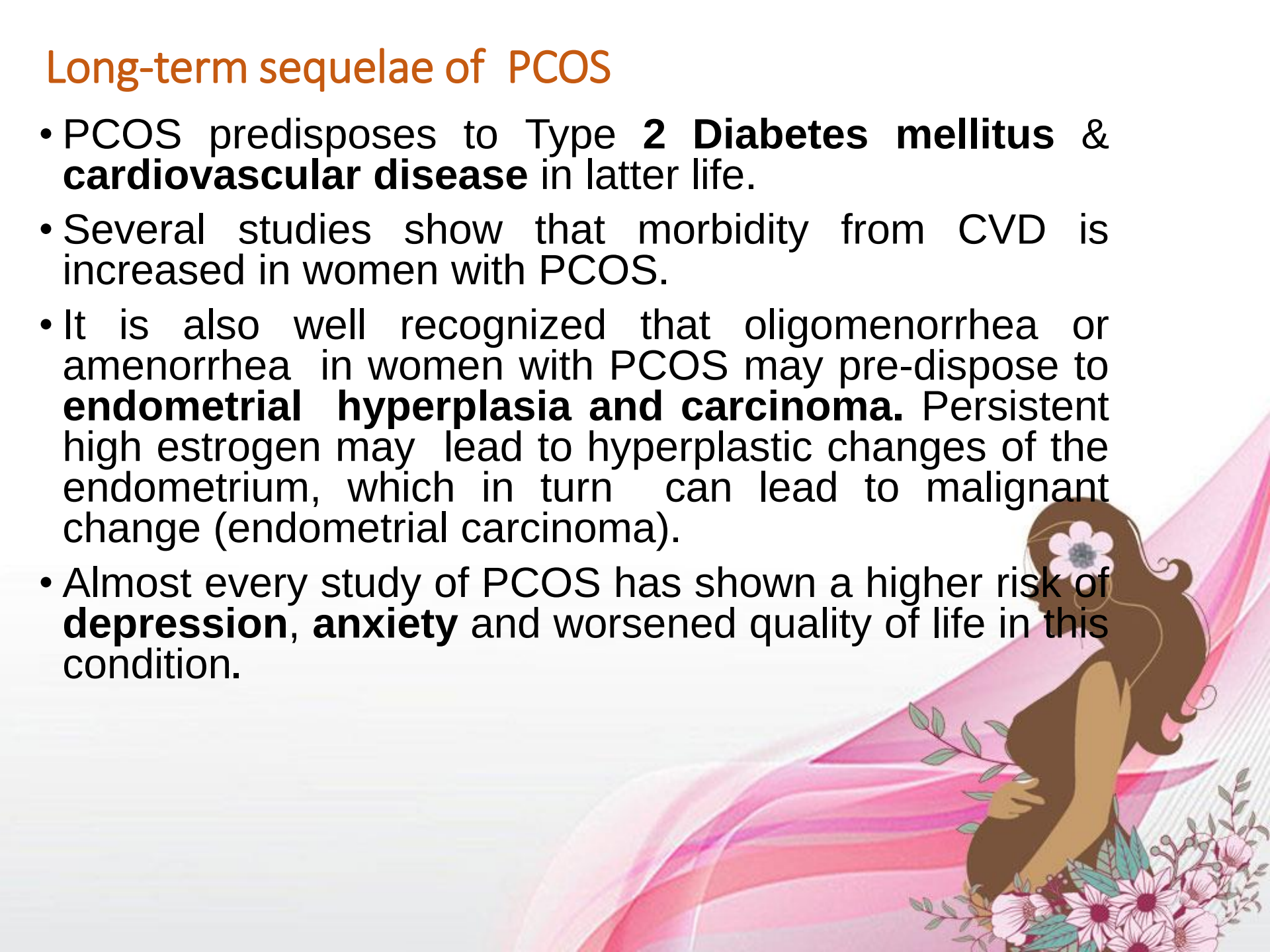
HIGH TESTOSTERONE LEVELS

ACNE

POLYCYSTIC OVARY SYNDROMS (PCOS)

Long-term sequelae of PCOS

- PCOS predisposes to Type **2 Diabetes mellitus** & **cardiovascular disease** in latter life.
- Several studies show that morbidity from CVD is increased in women with PCOS.
- It is also well recognized that oligomenorrhea or amenorrhea in women with PCOS may pre-dispose to **endometrial hyperplasia and carcinoma.** Persistent high estrogen may lead to hyperplastic changes of the endometrium, which in turn can lead to malignant change (endometrial carcinoma).
- Almost every study of PCOS has shown a higher risk of **depression**, **anxiety** and worsened quality of life in this condition.



Diagnosis Of PCOS (Rotterdam Criteria 2003)

(Two Of Three Criteria Needed)

- Oligomenorrhoea / amenorrhea (chronic anovulation).
- Clinical or biochemical hyperandrogenism.
- Polycystic ovaries:

Definition of polycystic ovary: Presence of at least 12 follicles measuring 2-9 mm in diameter and/or an ovarian volume in excess of 10 cm3 (usually obtained by ultrasound scan).

Laboratory tests

- Total and free testosterone levels: Elevated testosterone levels.
- Decreased SHBG levels.
- Free androgen index: Raised
- Androstenedione level.
- DHEAS.
- High LH levels.
- Elevated LH/FSH ratio.
- AMH.
- Fasting insulin levels: Increased
- Glucose level.
- Lipid profile.

Laboratory tests

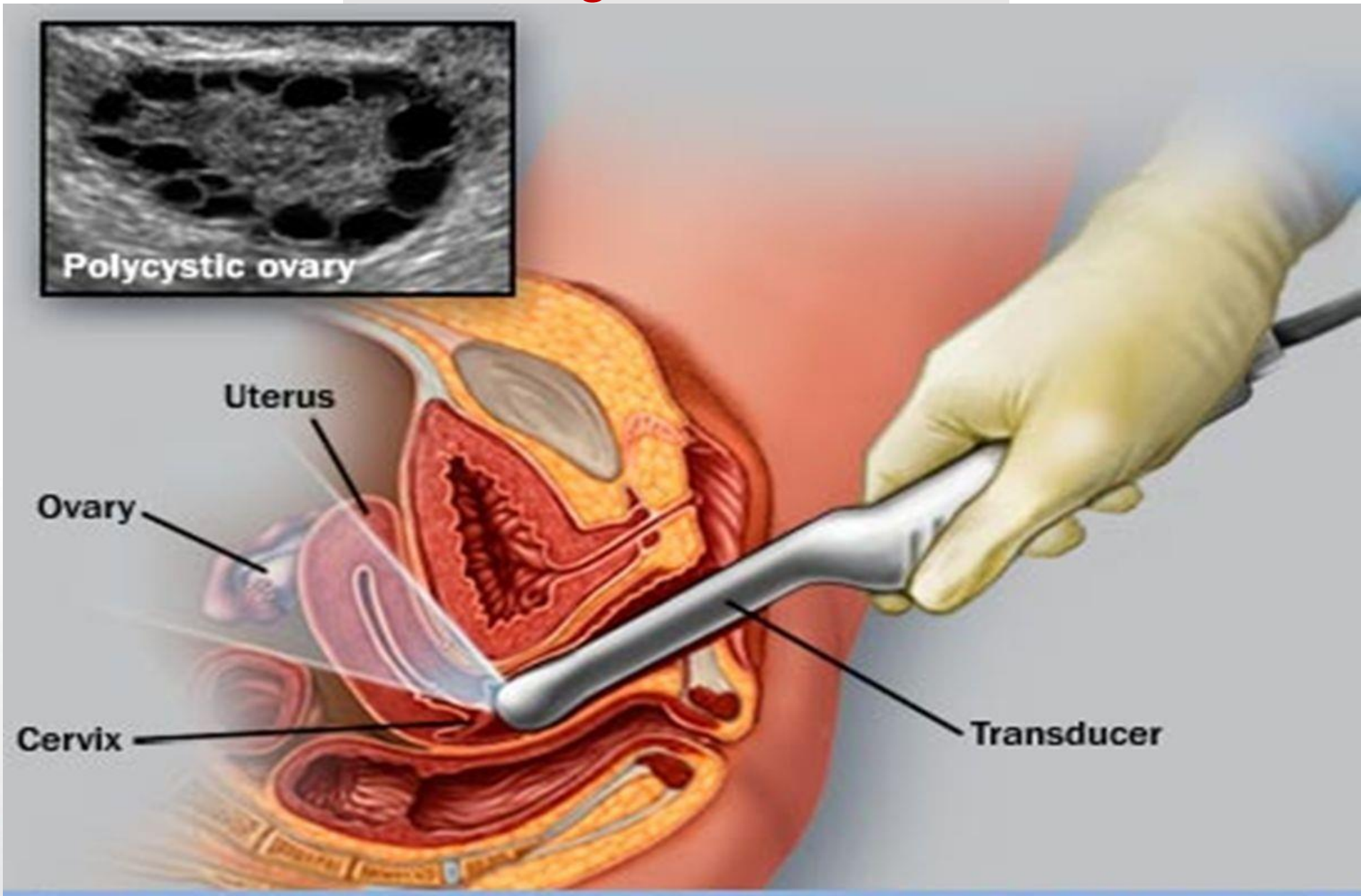
- Baseline screening laboratory studies for women suspected of having PCOS include the following:
- Thyroid function tests (eg, TSH, free thyroxine)
- Serum prolactin level
- Serum 17-hydroxyprogesterone (17-OHPG) level
- Urinary free cortisol (UFC) and creatinine levels
- Low-dose dexamethasone suppression test.

Imaging

- **Ovarian ultrasonography, preferably using transvaginal approach.**

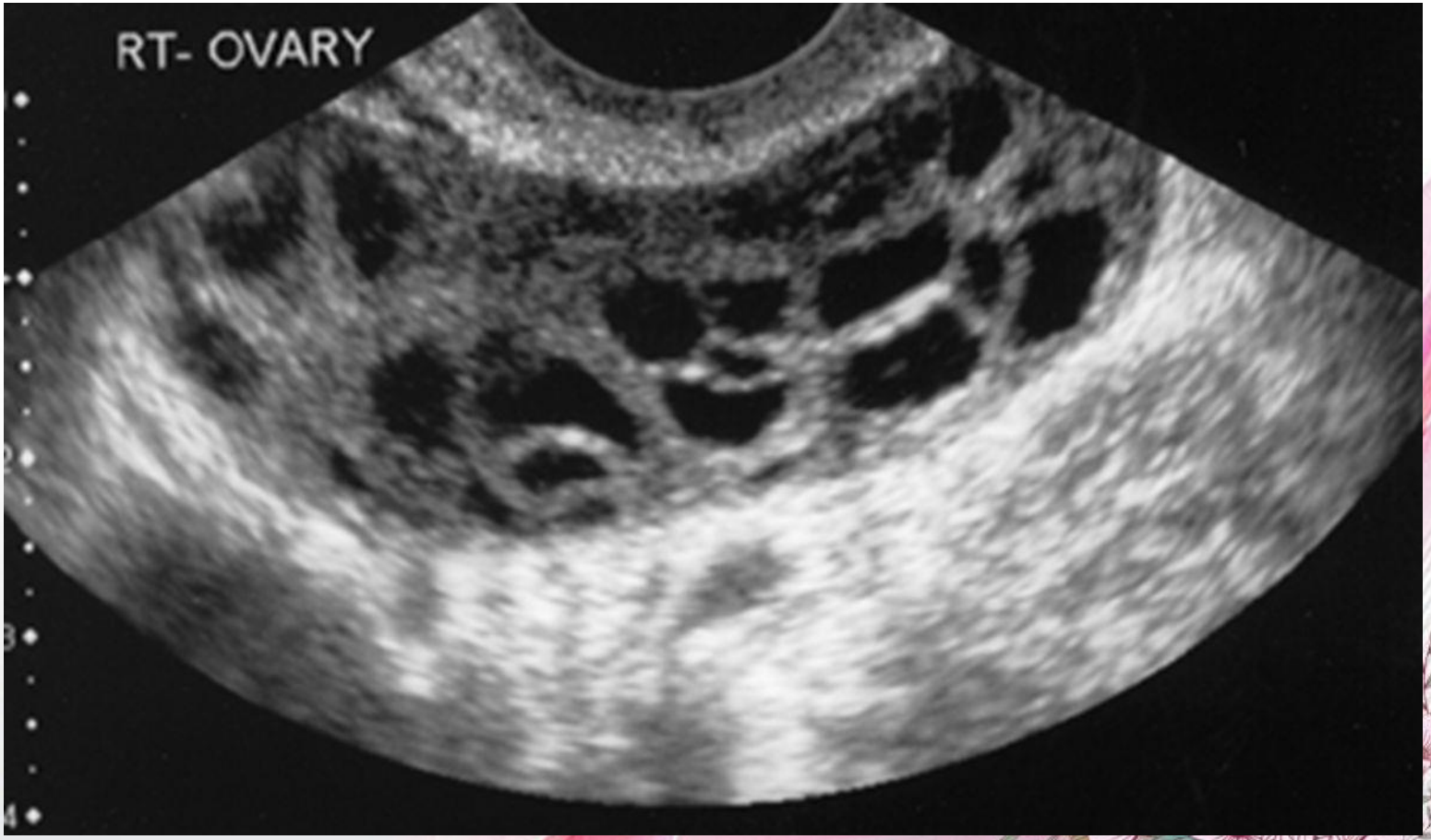
- **Pelvic CT scan or MRI to visualize the adrenals and ovaries.**

Transvaginal ultrasound



Ultrasound

U/S criteria for diagnosis of PCO .(Rotterdam Criteria by U/S)



Treatment

- **Individualized:**

To patient symptoms and complains .

Treatment

- Lifestyle modifications are considered first-line treatment for women with PCOS.

Include the following:

- Diet
- Exercise
- Weight loss
- Smoking cessation

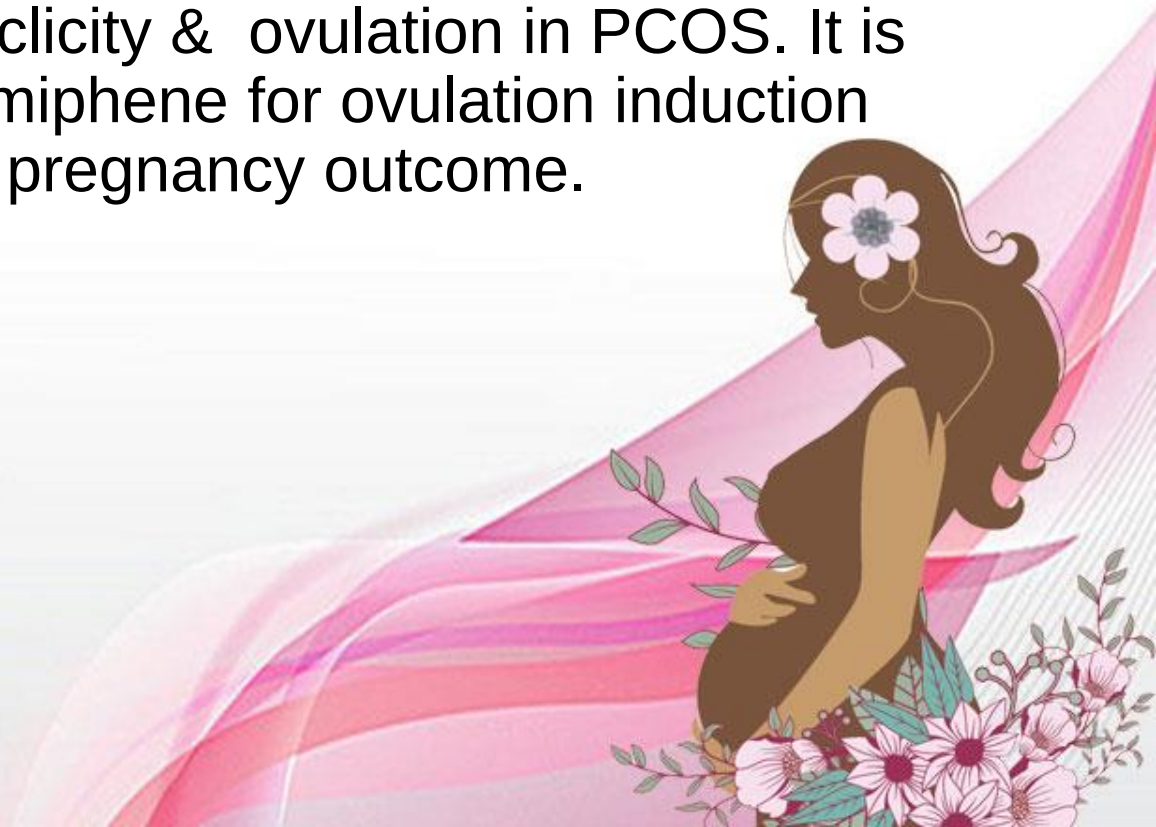
Treatment
Oligomenorrhoea/Amenorrhea

- Women with PCOS tend to be anovulatory but with normal or high estrogen levels. Without treatment there is theoretical risk of unopposed estrogen & endometrial cancer.

- Cyclical Progesterone induce regular menstruation and to protect endometrium. e.g. MPA- 10mg daily for 10 days.

- Oral contraceptive pill is an alternative treatment.

- Metformin- an oral biguanide, a drug that increases insulin sensitivity & there is a clear evidence that it improves menstrual cyclicity & ovulation in PCOS. It is less effective than clomiphene for ovulation induction and does not improve pregnancy outcome.



Hirsutism

- **Treatment aimed at reducing testosterone levels, this will not restore the hair to its pre-PCOS pattern but will slow the rate of hair growth.**

Options of treatment include the following:

1. **Cyproterone acetate:** A potent progestational, anti-androgen that competitively inhibits the androgen receptor.

- The combined preparations available are:

  Dianette /Diane-35 (2mg Cyproterone with 35micrograms Ethinyl -estradiol, EE), which can also be used for contraception.

Hirsutism

2.Yasmin: Contain progestagen, drosperinone, that has an anti-androgen effect through:

- Inhibition of ovarian androgen production.
- Blockage of androgen receptors.

3.Metformin: As an insulin sensitizing agent. It improves parameters of insulin resistance, hyperandrogenaemia,anovulation and acne in PCOS.

Hirsutism

4.Local treatment:

- Mechanical depilation.
- Electrolysis.
- Eflornithine hydrochloride 13.9% cream (Vaniqua™) Applied topically. Eflornithine is believed to block **ornithine decarboxylase** ODC & slow the differentiation of the cell within the hair follicles.

Subfertility

- Anovulation seen in association with (**PCOS).**
- Treatment options are Ovulation induction.
- Letrozole (aromatase inhibitor) as the first line treatment for ovulation induction in women with Polycystic Ovarian Syndrome (PCOS) due to data demonstrating increased ovulation rates, clinical pregnancy rates and live-birth rate vs clomiphene citrate.
- Lifestyle modification and weight loss are strongly encouraged along with letrozole therapy.

Subfertility

- Clomiphene Citrate: an antioestrogen medication, administered during follicular phase of menstrual cycle. It act by increasing gonadotrophin release from the pituitary, leading to enhanced follicular recruitment & growth. It is effective in inducing ovulation in 85% of women. It is recommended that treatment are monitered with serial U/S scans to minimize the risk of multiple pregnancy & risk of OHSS.
- Women who ovulate but do not become pregnant after 6 months of treatment may be offered clomiphene citrate-stimulated IUI.
- Tamoxifen.

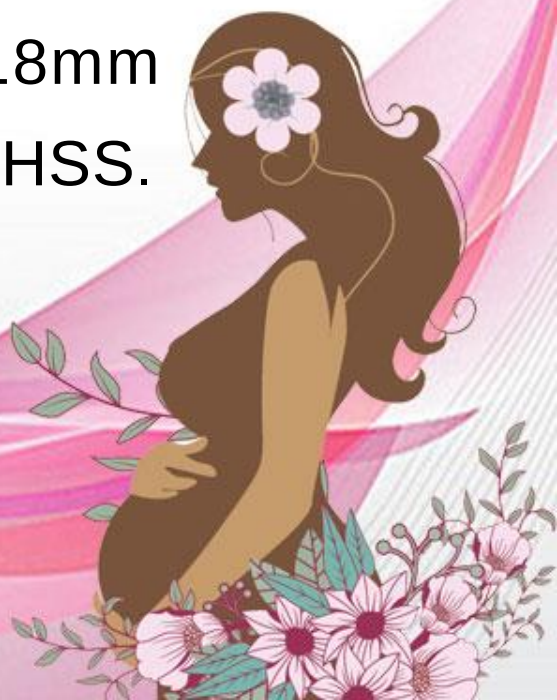
Subfertility

Metformin:

The combined approach of Metformin and Clomiphene citrate is better than Metformin monotherapy for inducing ovulation.

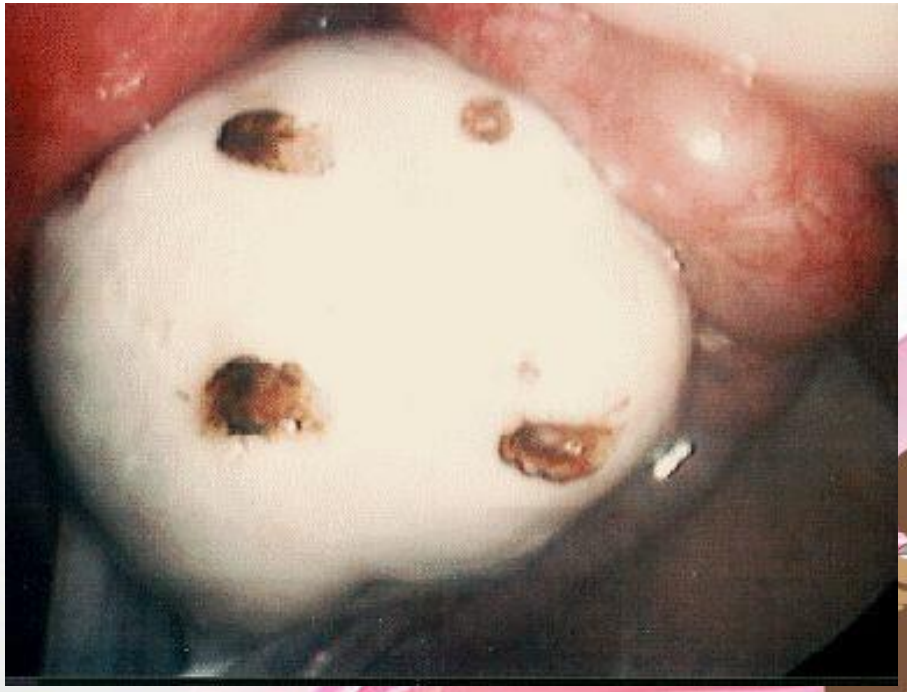
Subfertility

- Exoginous Gonadotrophins as ovulation induction. Dose is titrated against individual response & is monitered by U/S assessment of follicular number & size. Ovulation is triggered by hCG injection when 1-3 follicles are 18mm diameter. Risks of multiple pregnancy & OHSS.



Laparoscopic Ovarian Drilling (LOD):

A laparoscopic procedure to destroy some of the ovarian stroma that may prompt ovulatory cycles. Diathermy needle is used laparoscopically to make punctures in the surface of each ovary. It is as effective as Gonadotrophins, with no risk of OHSS, multiple pregnancies are less likely with OD



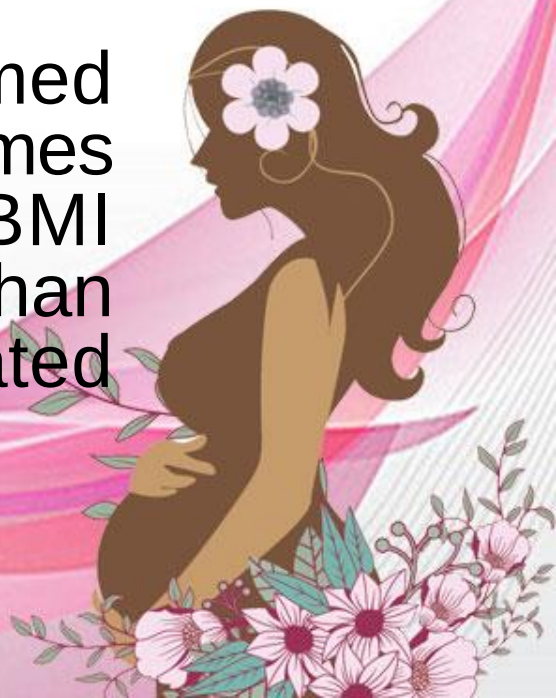
Obesity

- Weight reduction by dietary modifications with or without drugs may be considered.
- Weight-reduction drugs, e.g. orlistat (a lipase inhibitor), significantly reduce body weight and hyperandrogenism.
- Additionally, there is some evidence that metformin may be associated with a small reduction in BMI in women with PCOS.

Obesity

- Bariatric surgery has been shown to be effective in women with PCOS and may be an option for severely obese women with PCOS in whom long-term diet-based strategies are seldom successful.

- Bariatric surgery should be performed only when standard weight loss regimes have failed in PCOS women with a BMI greater than 40kg/m2 or greater than 35kg/m2 with a high-risk obesity related condition.



THANK YOU