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PCOS

Polycystic Ovary Syndrome



- Stein and Leventhal : 1935
- Since then our understanding of the disorders involved in the condition has evolved dramatically.

Significance and genetics

- Common endocrine disorder
- A leading cause of infertility
- May have a profound adverse impact on the health-related quality of life (HRQOL).
- Tends to cluster in families, and multiple candidate genes have been implicated.
 - Chromosome 19p13.3 as the likely candidate.
 - The same chromosome responsible for premature male balding

Prevalence

- 5-10% % of women worldwide, 25% of IVF patients.
- higher in certain ethnic groups, e.g. South Asians
- PCOS is higher in those with:
 - gestational diabetes.
 - premature adrenarche
 - in those with first-degree relatives who have PCOS

Criteria for Defining PCOS

- **ESHRE/ASRM (Rotterdam) 2003**

Two of the following in addition to exclusion of related disorders:

- Oligo and/or anovulation
- Hyperandrogenism and/or hyperandrogenemia
- PCO on U/S

≥12 follicles in each ovary, 2-9mm and/or
↑ ovarian volume (>10ml)

Diagnostic criteria

NIH (United States National Institutes of Health) 1990.

oligo-ovulation or anovulation (oligomenorrhea, amenorrhea)

hyperandrogenism (clinical or/and biochemical evidence of androgen excess)

exclusion of other disorders (menstrual irreg., hyperandrogenism)

The Androgen Excess and PCOS Society (AE-PCOS) 2006.

Oligo-ovulation and/or polycystic ovaries



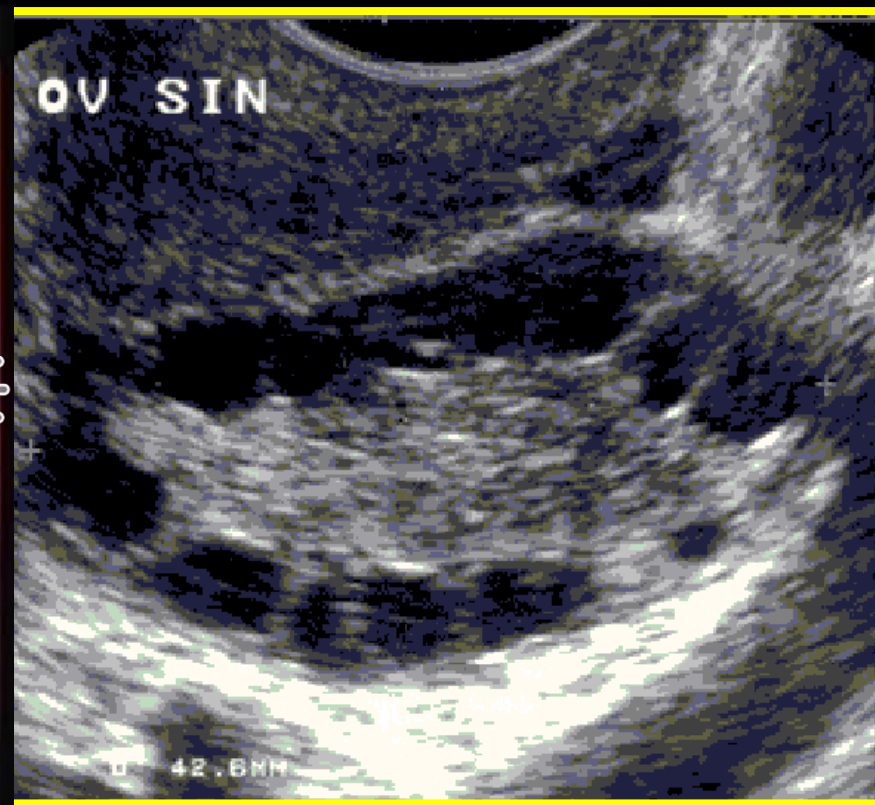
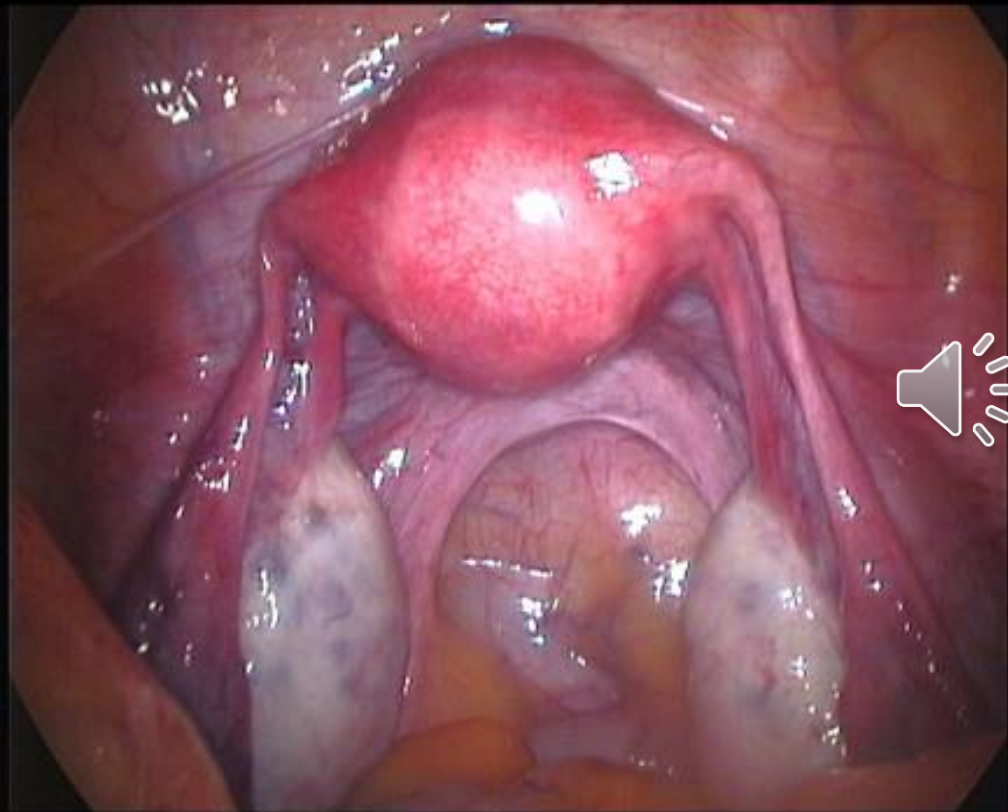
Clinical/biochemical evidence of hyperandrogenism

Exclusion of related disorders

PCOS, Rotterdam-criteria 2003 (ESHRE/ASRM)

Diagnosed when 2 of the 3 criterions fulfilled:

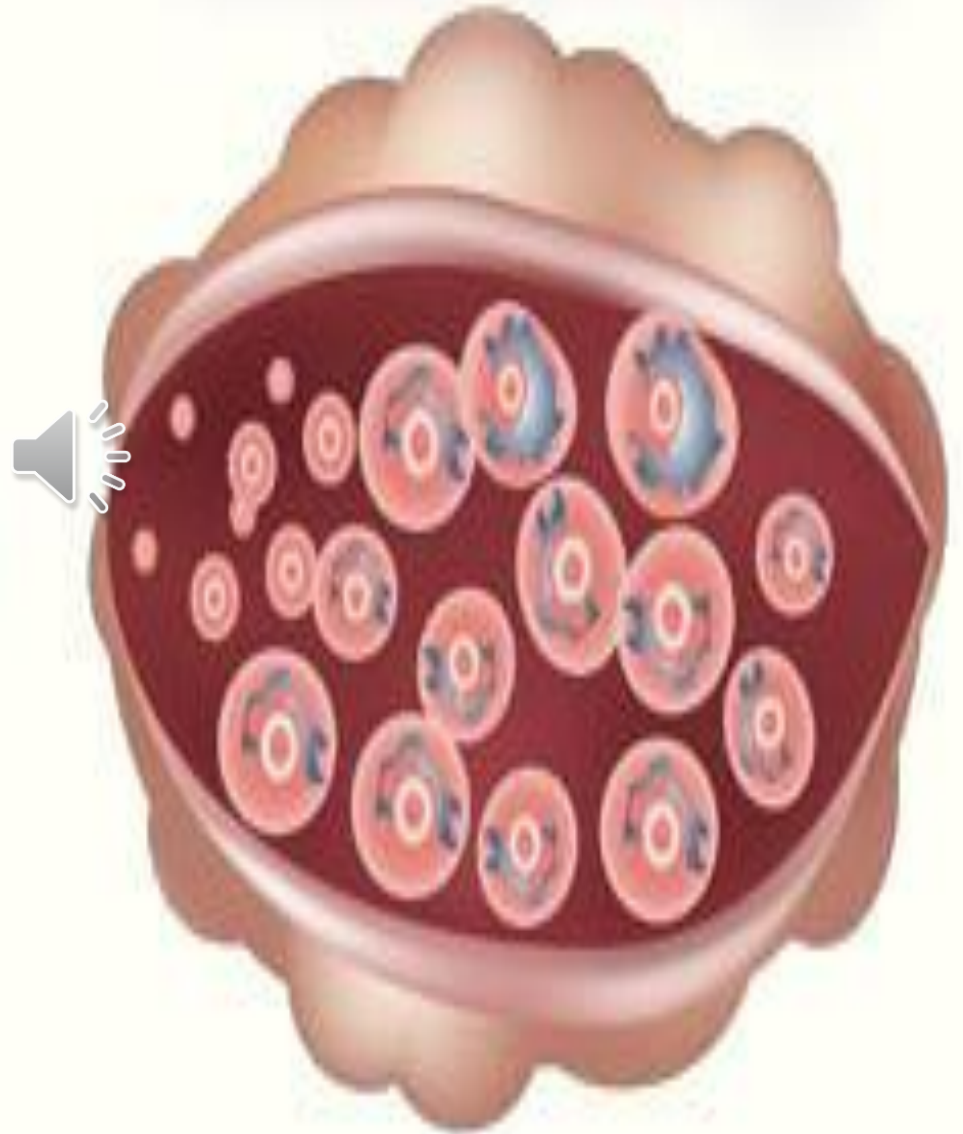
1. chronic anovulation (oligo- or amenorrhea)
2. Clinical and/or biochemical hyperandrogenism
3. polycystic ovaries



Normal ovary



Polycystic ovary



Aetiology

- Unknown
- PCOS is a multifactorial and polygenic.....
A.D?? 40% family Hx.




..... Hyperinsulinaemia and hyperandrogenism
are in the heart of this condition!!!!!!

Pathophysiology

- Dysfunction in ovarian function leading to **increase androgen** production....arising from **exaggerated response of LH by theca cells** and augmented by the **effect of insulin binding to IGF-1&2** (important regulator for follicular maturation and steroidogenesis)
- Dysfunction in hypothalamic function leading to **increased LH** which stimulates androgen production
- **Insulin resistance...** From phosphorylation of tyrosine and serine residues on receptorsleading to compensatory hyperinsulinaemia , that also ↓ hepatic production of IGF-1&2 BP.... that will ↑ the bioavailability of IGF-1&2

Insulin resistance

- Insulin stimulates **androgen production** from ovary and adrenal and may alter gonadotrophin secretion.
- ↓ **SHBG** synthesis in the  liver thus ↑ free testosterone
- In patients with PCOS, there is selective tissue insulin sensitivity (skeletal muscle is resistant but ovary and adrenal are sensitive).

Other manifestations of PCOS

- **Obesity**

≥ 50% of PCOS patients

- **Metabolic syndrome**


Type 2 Diabetes, HTN,  dyslipidaemia, atherosclerosis & IHD

- **Dermatological**


Hirsutism, oily skin, acne, alopecia

Acanthosis nigricans

Long term effects

- Obesity
- DM
- Cardiovascular diseases.
- Ca endometrium 
- PCOS and pregnancy
- Hirsutism
- Infertility


Obesity

- $\geq 50\%$ of patients with PCOS
- Most often a **central** obesity with an **android** appearance and an increased waist-to-hip ratio 
- Related to **insulin resistance**.
- Women with PCOS find it more difficult to lose weight and appear to gain weight more easily.


Treatment of Obesity

- Lifestyle changes
- Pharmacological agents
 1. Centrally acting serotonin & norepinephrine uptake inhibitor, **Sibutramine**
 2. Peripherally acting lipase inhibitor, **Orlistat**
- **Bariatric surgery**

Work up

- **TSH**
- **FBS and lipid profile**
- **PRL** elevated in 40% of patients with PCOS, secondary to stimulation of the prolactin-producing cells by chronic oestrogen and not related to the cause of the disease state 
- **Free androgen index**
- **FSH and oestradiol** to exclude the possibility of premature ovarian failure
 - FSH should be elevated greater than 25 pg/mL.
 - Associated with a suppressed oestradiol less than 30 pg/mL

Management of PCOS

- Treatment depends on **needs** of patient and preventing **long term** health problems
- **Weight reduction** results in improvement in all symptoms of PCOS  10% wt. Loss will restore normal hormones level and spontaneous ovulation in 40% of women.

Ovulation induction

- . Metformine.... Ovulation rate is 8%
- Anti-oestrogens....e.g. Clomiphen citrate..
75% will ovulate within 6 months.
- Gonadotropins (Risk of M.P & OHSS 15% in PCOS vs. 0.3-5% non-PCOS)
- Aromatase inhibitors...for clomid ROS (25%)
- Pulsatile GnRH.....?????????


Insulin sensitizing agents

Metformin

- If $\text{BMI} \geq 25$????????, life long
- Pregnancy rate 8%
- Weight loss- controversial
- Safe if continued into the 1st trimester, may decrease the risk of miscarriage in obese pts

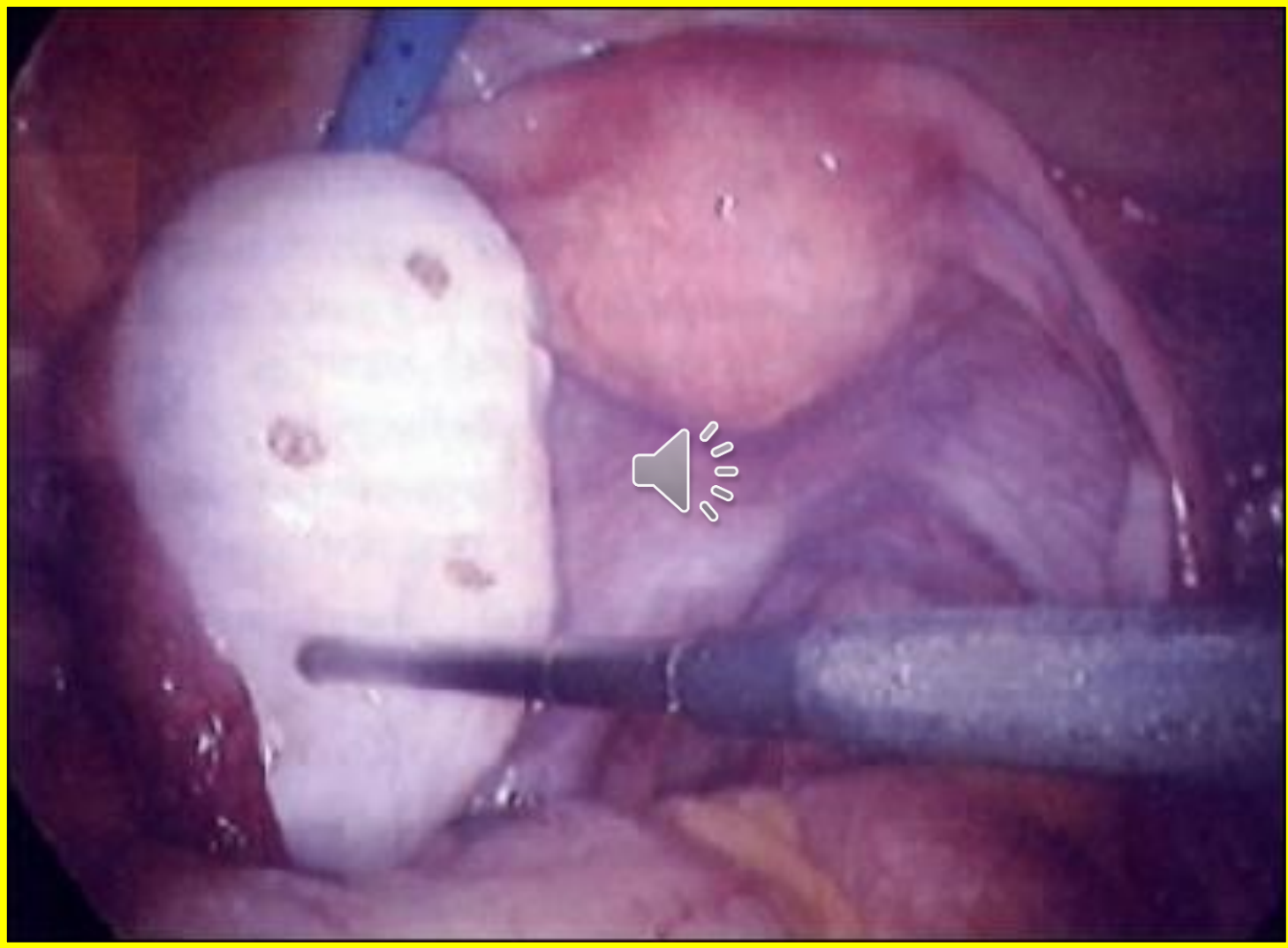
Laparoscopic ovarian drilling

LOD

- When medical Rx. failed
- 4 punctures , 2–4 mm deep in the cortex of each ovary. 40 W for 4 seconds
- Ovulation rate of 80% & clinical pregnancy 60%
- Mechanism unknown,  destruction of luteinized follicles??
- Thermal damage leads to release of inflammatory intra-ovarian cytokines

Cont.

- . LOD has a similar outcome to Gonadotropins in term of Ovulation and pregnancy rate, but it's preferred option because it is free of side effects of gonadotropins(MP&OHSS)
- . Long term consequences.....POF, no any evidence.
- . Cheaper overall



Thank you