Female Reproductive Endocrinology

Dr. Channa Jayasena PhD MRCP FRCPath
Clinical Senior Lecturer & Consultant Endocrinologist
Department of Gynaecology, Hammersmith Hospital

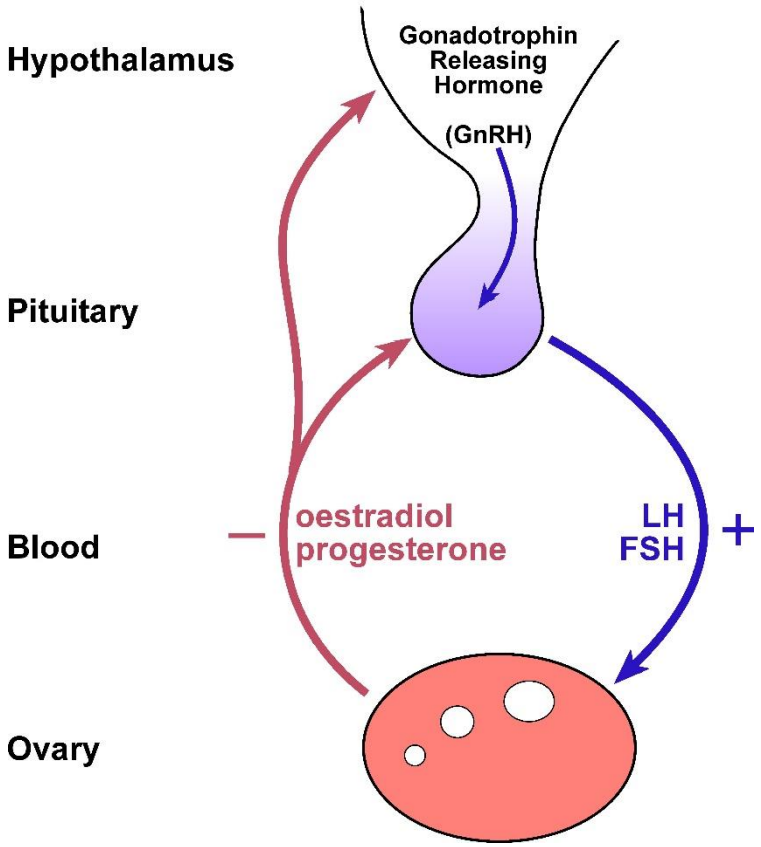
Anovulation is a common cause of infertility

- **Disorders of ovulation account for about 25% of causes of infertility**
- **Most are due to abnormal endocrine environment**
- **Most are treatable**

Presentation of anovulation

- **Amenorrhoea (primary or secondary)**
- **Oligomenorrhoea (cycle >42 days)**
- **Irregular menses (e.g. cycles varying between 2 and 6 weeks in duration)**

Female reproductive axis



Causes of anovulation

- PCOS (60%)
- Functional hypothalamic amenorrhoea (20%)
- Prolactinoma (10%)
- Hyper- or hypothyroidism (5%)
- Non-functioning adenoma
- If shorter history, exclude pregnancy

Investigation of anovulation

- FSH, LH
- Prolactin (if amenorrhoea)
- Serum oestradiol
- TFTs
- Pelvic ultrasound
  - Endometrial thickness
  - Polycystic ovaries

AR aged 27 years

- 1 year history of secondary amenorrhoea - hoping to conceive
- No history of weight change
- Previous history of OCP use (but periods resumed after stopping)
- Examination unremarkable; BMI 23

Investigations:

FSH 2.8 iu/l (3 -11)

LH 1.2 iu/l (3 -11)

Prolactin 3,500 mU/l (50-500)

Progress:

Repeat prolactin 3,700 mU/l

TSH 2.6 mU/l (0.5 - 5.0)

MRI - microadenoma

Management: dopamine agonists

Started on bromocriptine 2.5 mg bd

- **Suppression of prolactin to normal within 2 weeks**
- **Menses returned within 6 weeks**
- **Pregnant after 3 months of treatment**

Polycystic ovarian syndrome

Clinical Diagnosis:

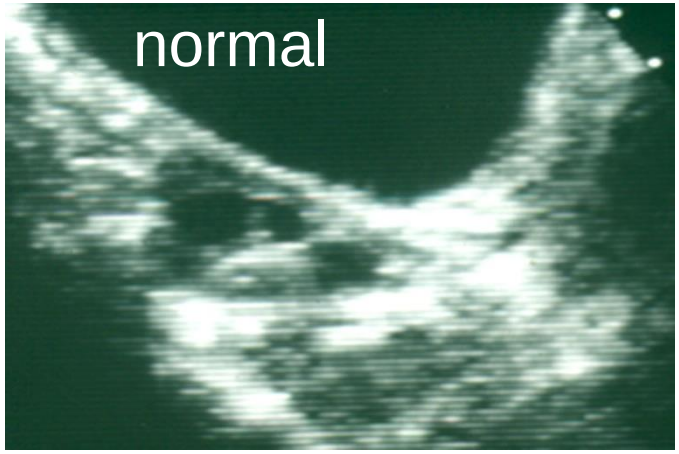
- Clinical or biochemical hyperandrogenaemia
- Anovulation
- Polycystic ovaries

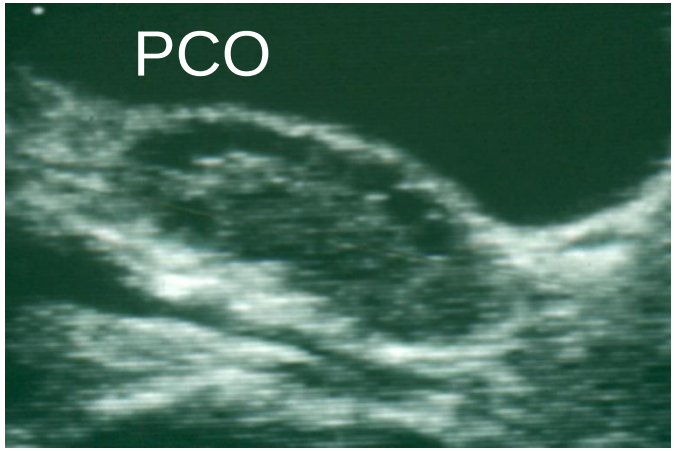
Rotterdam

Blood tests:

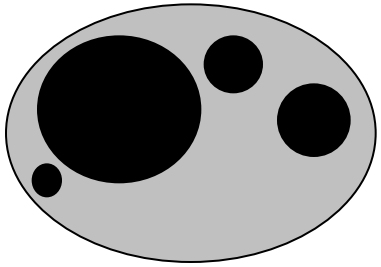
- E2: exclude hypogonadism
- Testosterone
- TFT
- Prolactin
- OGTT if FHx or overweight

Polycystic ovary

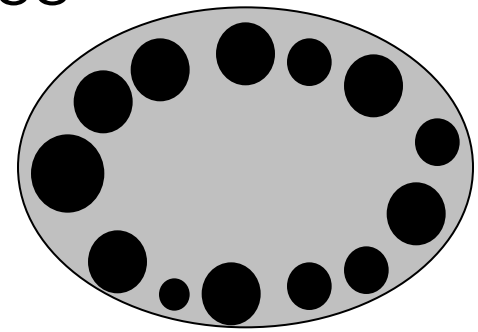




normal

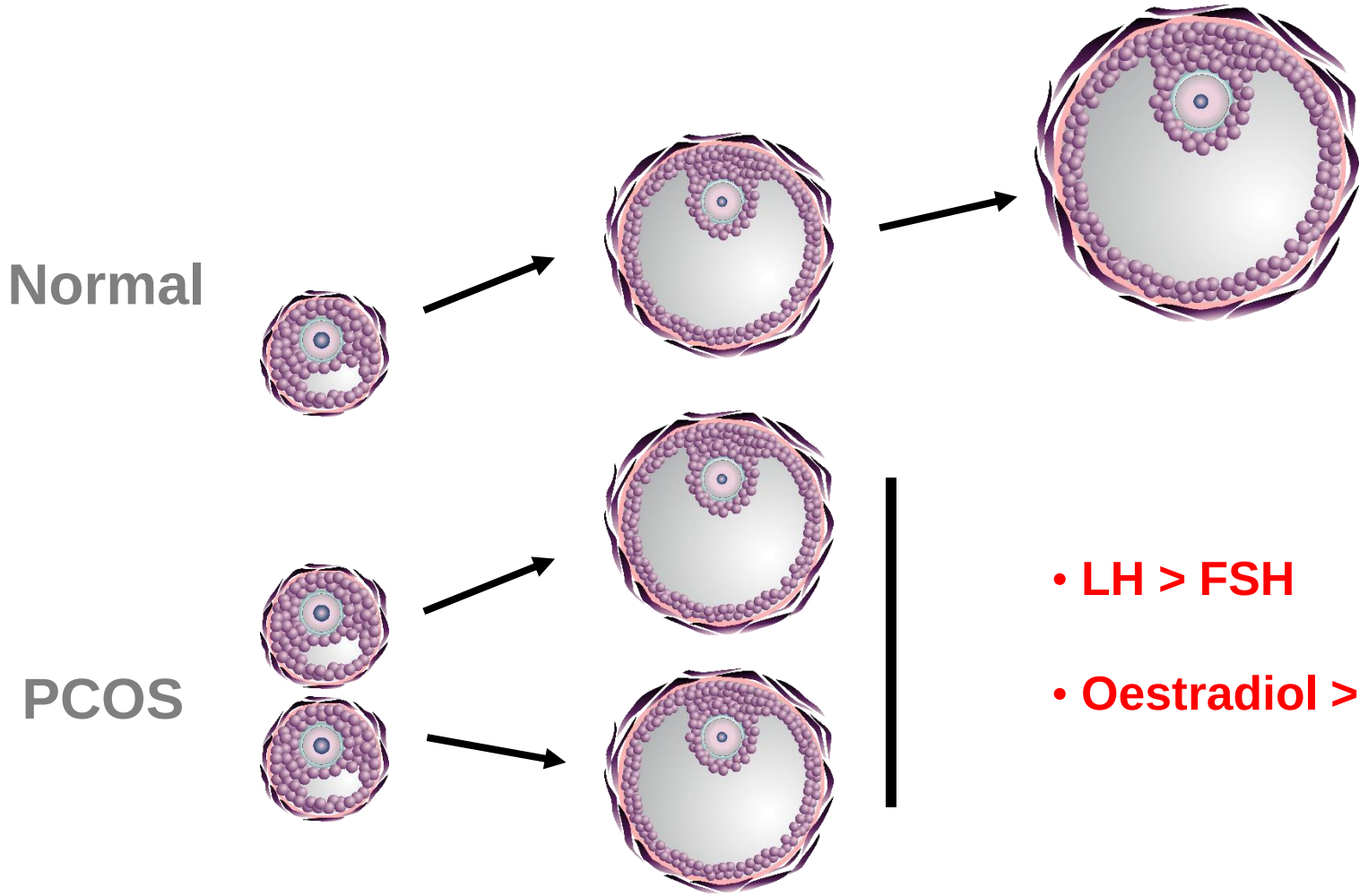


PCO



more follicles, more stroma

Arrested antral follicle development in PCOS



What is your patient's treatment priority?

PCOS: Mainly androgenic symptoms

PCOS: Main problem is periods

PCOS: Main problem is infertility

PCOS: Mainly androgenic symptoms

- **Weight loss**
- **Cosmetic treatment**
- **All types of OCP suppress endogenous androgens**
  - **Migraines – caused by E2**
  - **Low mood– caused by P**
  - **Gastric symptoms – caused by P**
- **2nd line.**
  - **Spironolactone**
  - **Anti-androgen**
- **Metformin will not help**

PCOS: Main problem is periods

- **Weight loss + exercise** is highly effective if overweight

- **OCP**

  Wants regular bleeds: Cyclical E2 + P

  Does not want bleed: Continuous E2 + P OCP

- Metformin has slight effect only
  - Ideal for glucose intolerance / DM

PCOS: Main problem is infertility

- **Weight loss + exercise** is highly effective (but difficult)
- **Bariatric surgery** if required
- **Reassure** Average 1.8 children per patient (normal = 2.2 in UK)
- **Ovulation induction** (clomiphene or FSH) or IVF

24y woman

- **Secondary amenorrhoea.**
- **Also some acne.**
- **Menarche aged 12y, with regular periods till went on OCP aged 16y.**
- **Stopped OCP 2y ago, and no periods since then**
- **No medications or concurrent medical problems**
- **No galactorrhoea**

24y women: secondary amenorrhoea

- **Mild ongoing acne on face**
- **Waxes facial hair once per month, but no chest or back acne or excessive hair**
- **No recent weight loss / Hx eating disorders**
- **Exercise: 3h per week in gym**

On examination

- **Weight 54kg. BMI 21.6kg/m2**
- **Evidence of mild facial acne**
- **No hirsutism**

What is the differential diagnosis?

Differential: secondary amenorrhoea in a woman < 40 years old

- **PCOS (60%)**
- **Functional hypothalamic amenorrhoea (20%)**
- **Prolactinoma (10%)**
- **Hyper- or hypothyroidism (5%)**
- **Non-functioning adenoma**
- **If shorter history, exclude pregnancy**

What investigations would you do?

- **LH 0.5iU/L**
- **FSH 3.6iU/L**
- **Oestradiol <70pmol/L**
- **Testosterone: 0.8nmol/L**
- **Prolactin 187. TSH 1.01. FT4 10.2**
- **Ultrasound : multiple cysts in L. and R. ovaries. 2mm endometrial thickness.**

Do the results suggest PCOS?

Hypothalamic amenorrhoea (probably functional)

- LH 0.5iU/L
- FSH 3.6iU/L
- **Oestradiol <70pmol/L**
- Testosterone: 0.8nmol/L
- Prolactin 187. TSH 1.01. FT4 10.2
- Ultrasound : lots of cysts in R. ovary. L. ovary normal. **2mm endometrial thickness.**

This patients has hypogonadism, which is incompatible with diagnosis of PCOS

Hypothalamic amenorrhoea (probably functional)

- **Acquired loss of GnRH secretion caused by:**
  - **Weight loss**
  - **Exercise**
  - **Psychological stress**
- **Often resolves spontaneously**
- **Rx: E2 replacement / reduce exercise / psychological**
- **Refer if psychiatric disease / needs ovulation induction**

Functional HA

- BMI usually <23kg/m2
- Acne / hirsutism can be seen
- Polycystic ovarian appearances: possible
- **E2 <100 pmol/L**
- **LH < 5iU/L**
- **FSH > LH**

PCOS

- BMI can be normal or high
- Acne / hirsutism can be seen
- Polycystic ovarian appearances: possible .
- **E2 higher**
- **LH > 5iU/L**
- **LH > FSH**

Case 2: Secondary amenorrhoea

- 28y woman
- BMI 24.5kg/m2
- Menarche aged 13y, periods ‘like clock-work’ every 30d
- 15/12 ago, periods less regular and frequent.
- Amenorrhoea for last 6/12

Blood tests

TEST	MARCH ’17
Serum LH (iU/L)	12
Serum FSH (iU/L)	19
Serum E2 (pmol/L)	108

Blood tests

TEST	MARCH ’17	JUNE ‘17
Serum LH (iU/L)	12	24
Serum FSH (iU/L)	19	42
Serum E2 (pmol/L)	108	<70

Blood tests

TEST	MARCH ’17	JUNE ‘17	DEC ‘17
Serum LH (iU/L)	12	24	22
Serum FSH (iU/L)	19	42	39
Serum E2 (pmol/L)	108	<70	<70

What is the diagnosis?

Premature ovarian insufficiency

- **Age < 40 years**
- **Amenorrhoea > 4 months**
- **FSH > 25iU/L on two occasions**

POI affects 10% of women < 40 years
POI affects 1% of women < 30 years
POI affects 0.1% of women < 20 years

UK National Institute of Clinical Excellent (NICE) Guidelines 2015

Premature ovarian insufficiency

What is her chance of future pregnancy?

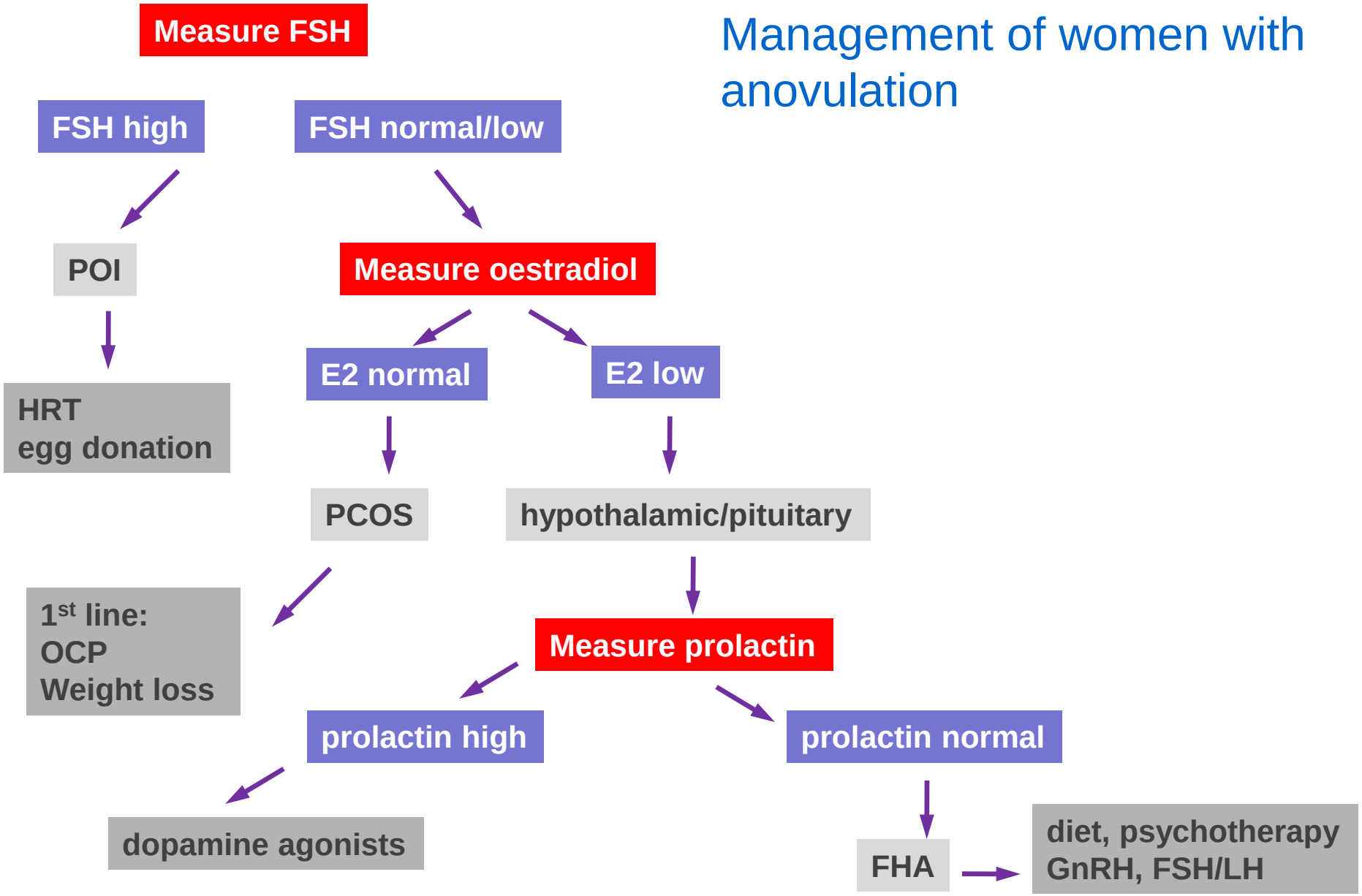
- 4.4% in retrospective French series (n=358)
- Occurred < 4y following diagnosis

What are her treatment options?

- IVF – highly inadvisable unless periods restart
- Egg donation increasingly popular

Bidet et al. JCEM 2011

Management of women with anovulation



Please contact us

Dr. Channa Jayasena
Ms. Lisa Webber
Prof. Stephen Franks

Channa.Jayasena@nhs.net