Current Evidence in Ovarian Reserve - PCOS

Dr. Rana Choudhary

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Masters in Reproductive Medicine (UK)

Diploma in Clinical Research

DESIGNATION:

- Consultant Obstetrician & Gynaecologist
- Reproductive Medicine Specialist
- Wockhardt hospital & Ankoor Fertility Clinic (Mumbai)

AWARDS:

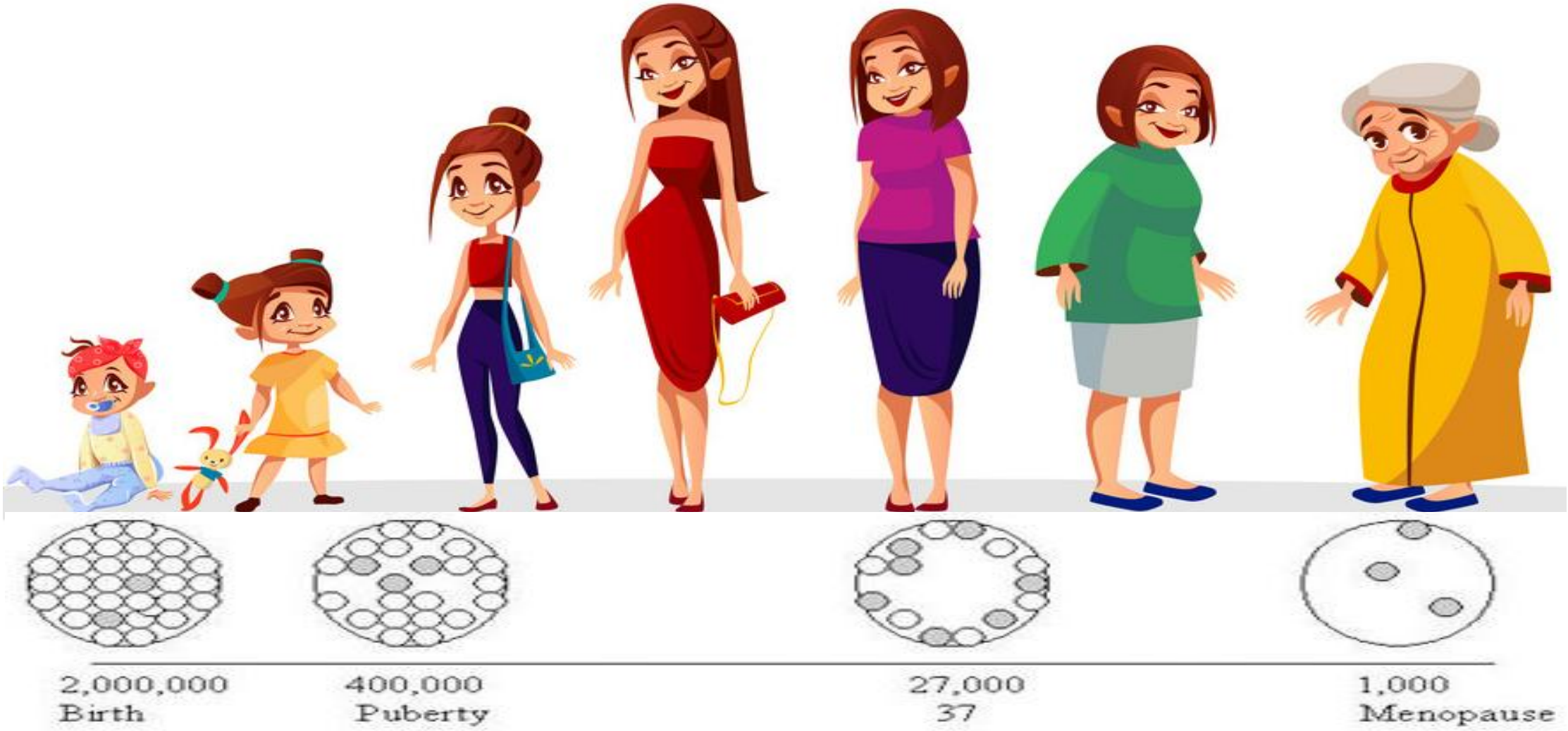
- FOGSI Future award, FOGSI Shanti Yadav award for Infertility,
- FOGSI Imaging science award
- MOGS Dr Pramila Bhatia Young Scientist award & Dr. H. Desa award
- Best Scientific paper award at various conferences

PUBLICATIONS: National & international publications

Peer reviewer of National & International journals

SPECIAL INTERESTS: Reproductive medicine & Infertility

Introduction



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Reshef Tal et al. Ovarian reserve testing: a user's guide. AJOG. August **2017**

Ovarian Reserve

Functional potential of ovary; reflects the number & quality of oocytes within it.

- Quantity of oocytes (ovarian age)
- Quality of oocytes (chronological age)

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Ovarian Reserve

- **Ovarian reserve -** Determine capacity of ovary to provide oocytes that are capable of fertilization resulting in a healthy & successful pregnancy
- Complex clinical phenomenon influenced by age, genetics & environmental variables
- Decline is irreversible & Rate varies considerably
- Ovarian reserve markers serve as a proxy for oocyte quantity but are considered poor predictors of oocyte quality

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Indications for ovarian reserve testing

Women undergoing infertility evaluation/treatment
Individualization of assisted reproductive technology ovarian stimulation protocol and dosing
History of premature ovarian failure (insufficiency) or early menopause
Polycystic ovarian syndrome
Women considering elective (social egg) freezing
Oocyte donors
Fertility preservation before and after gonadotoxic treatment
Preoperative prior to ovarian surgery in reproductive-age women
Diagnosis and recurrence surveillance for granulosa cell tumors
Perimenopause
Women with BRCA-1 or FMR1 premutation

BRCA-1, breast cancer gene-1; *FMR1*, fragile X mental retardation 1.

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ORT – Whom & Why?

WHOM:

- General Population
- Subfertile women
- IVF

WHY:

- Informed decision about childbearing
- Planning rapidity & mode of Rx
- Assess response & probability of pregnancy
- Limit attempts or exclude

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Markers of Ovarian Reserve

Age – > 36 Years (Basic Marker)

Basal Hormones

1. **FSH** *(Scott et al., 1989; Toner et al., 1991)*
2. Inhibin B *(Hall et al., 1999)*
3. **Anti-Mullerian Hormone** (AMH)

   (van Rooij et al., 2002)
4. Oestradiol

Sonographic Parameters

1. **Antral follicle count(AFC)** *(Bancsi et al., 2002; van Rooij et al., 2002)*
2. Ovarian volume
3. Ovarian vascular flow

Challenge tests/Dynamic tests

1. Clomiphene citrate challenge test (CCCT)
2. GnRH agonist stimulation test (GAST) *(Winslow et al., 1991)*
3. Exogenous FSH ovarian reserve test (EFORT) *(Fanchin et al., 1994)*

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Ideal ORT

- Predict conception (with or without treatment)
- Predict the time of onset of ovarian ageing
- Guide in selection of optimal dose of gonadotropins
- Easily measurable, minimally invasive, inexpensive & good predictive value
- Minimize risk of wrongly diagnosing as DOR
- Accurately identify those at greatest risk of developing OHSS
- Identify patients who will have poor response

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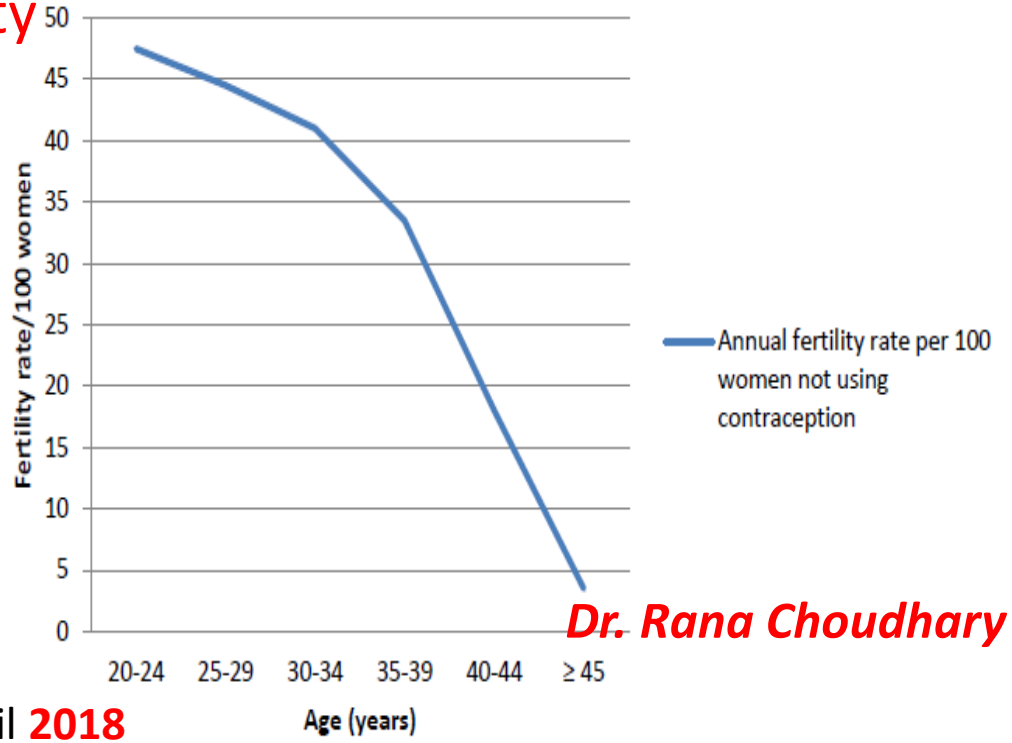
Reshef Tal et al. Ovarian reserve testing: a user's guide. AJOG. August **2017.**
Padma Rekah Jirge. Ovarian reserve tests. J Hum Reprod Sci. Dec **2011**

Age

- Ovarian reserve reduces progressively with age
- Most important factor determining pregnancy potential in regularly cycling women
- Age still remains the best predictor of oocyte quality
- Chronological age alone has a limited value in predicting individual ovarian responses

Figure 5.1 The effect of maternal age on the average rate of pregnancy, calculated on the basis of studies in10 different populations that did not use contraceptives (adapted from Heffner, 2004, based on two reviews by Menken et al, 1986, and Anderson et al, 2000)



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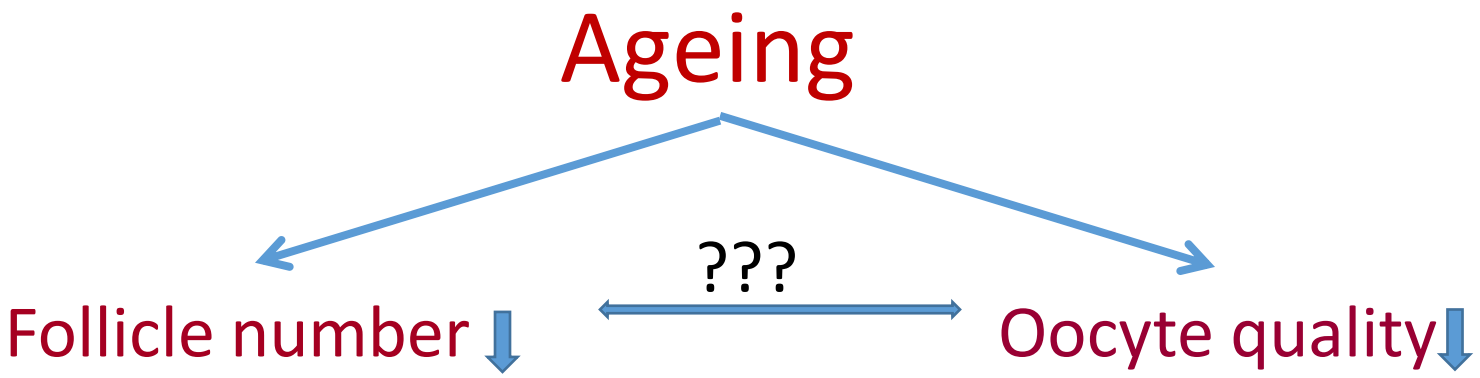
Assessing & managing ovulation disorders. **NICE** Pathway last updated: April **2018**

Ovarian reserve = Composite of follicle number & oocyte quality

(te Velde and Pearson, 2002)

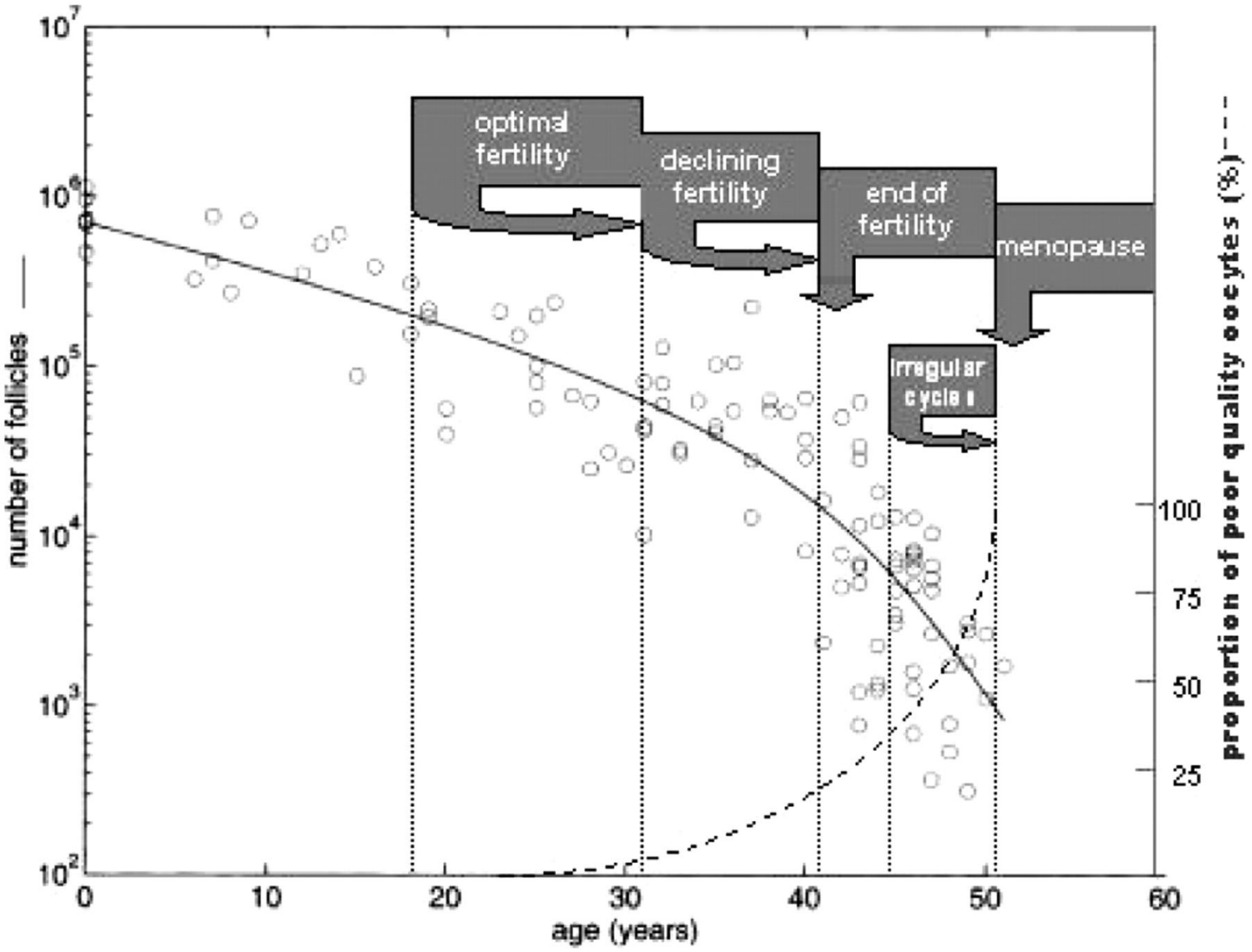


Change in fertilizability & Implantation potential

↑ risk of embryonic chromosomal abnormalities

↑ Spontaneous abortions

Quantitative (solid line) & qualitative (dotted line) decline of ovarian follicle pool, which is assumed to dictate onset of important reproductive events



Decline in fertility with age– quantitative & qualitative

Female age - important predictor of success in IVF treatment

Only ORT to predict probability of pregnancy

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Broekmans, F.J. et al. Hum Reprod Update **2006**

Comparison of ovarian reserve markers follicle-stimulating hormone, antral follicular count, and antimüllerian hormone

Test	Basal FSH	AFC	AMH
Year described	1988	1997	2002
Timing	Day 2–5 of menstrual cycle	Day 2–5 of menstrual cycle	Any day
Temporal change indicating ovarian aging	Latest	Early	Earliest
Intracycle variability	Clinically significant	Clinically significant	Minimal
Intercycle variability	Clinically significant	Minimal	Minimal
Methodology	Automated	Ultrasound	ELISA/automated
Cost, $	95–125	300–500	76–95

Reshef Tal et al. Ovarian reserve testing: a user's guide. AJOG. August 2017

Comparison of ovarian reserve markers follicle-stimulating hormone, antral follicular count, and antimüllerian hormone

Test	Basal FSH	AFC	AMH
Advantages	Widespread use	Immediate results; good predictive value for stimulation ovarian response, including predicting OHSS	Reliable; high sensitivity; good predictive value for stimulation ovarian response, including predicting OHSS
Limitations	Reliability; low sensitivity; dependent on functional HPO axis; less precision due to intercycle and intracycle variability; does not predict OHSS	Interobserver variability (sonographer-dependent); requires cost of ultrasound technician and availability of ultrasound machine; significant intercycle variation in overweight and obese	Lack of international standardized assay; requires careful sample preparation and storage

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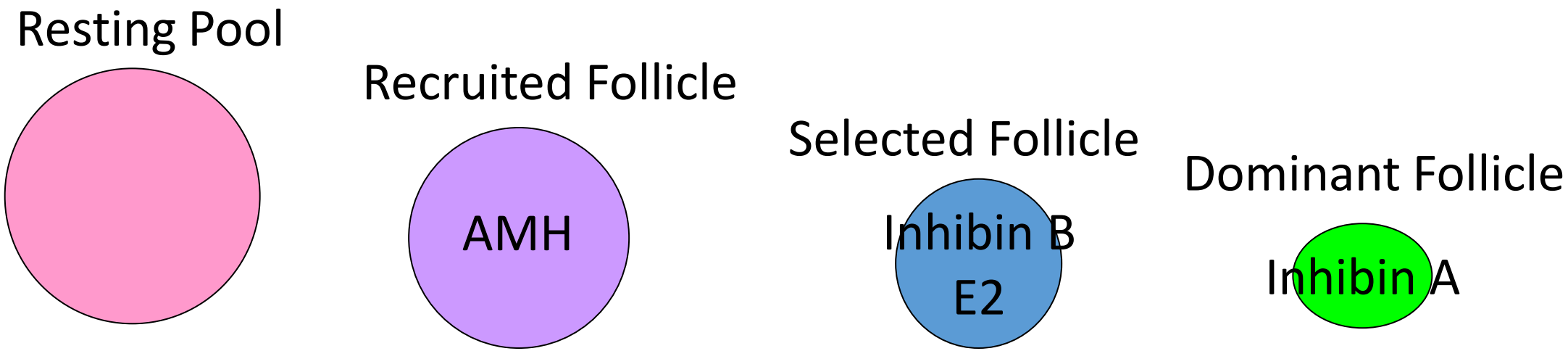
Reshef Tal et al. Ovarian reserve testing: a user's guide. AJOG. August **2017**

Comparison of ovarian reserve markers follicle-stimulating hormone, antral follicular count, and antimüllerian hormone

Test	Basal FSH	AFC	AMH
Cut-offs used for determining sensitivities and specificities	10–20 IU/L	<3–4 follicles (total)	0.1–1.66[a] ng/mL or <0.1–<0.3[b] ng/mL
Sensitivity for poor response, %	11–86[15]	9–73[15]	44–97[4]
Specificity for poor response, %	45–100[15]	73–97[15]	41–100[4]
AUC for poor response	0.68 (95% CI 0.61–0.74)[42]	0.76 (95% CI 0.70–0.82)[42]	0.78 (95% CI 0.72–0.84)[42]
Sensitivity for nonpregnancy, %	3–65[15]	7–34[15]	19–66[32]
Specificity for nonpregnancy, %	50–100[15]	64–98[15]	55–89[32]

Reshef Tal et al. Ovarian reserve testing: a user's guide. AJOG. August **2017**

Expression of OR markers



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Which ovarian reserve test to choose?

- AMH & AFC > FSH
- AMH - Direct product of both cumulus & mural granulosa cells from preantral & small antral follicles during early folliculogenesis
- AMH will decline years prior to a rise in FSH
- Earlier, More sensitive , Real time biomarker
- Greater correlation with primordial follicle pool
- Indirect markers – FSH

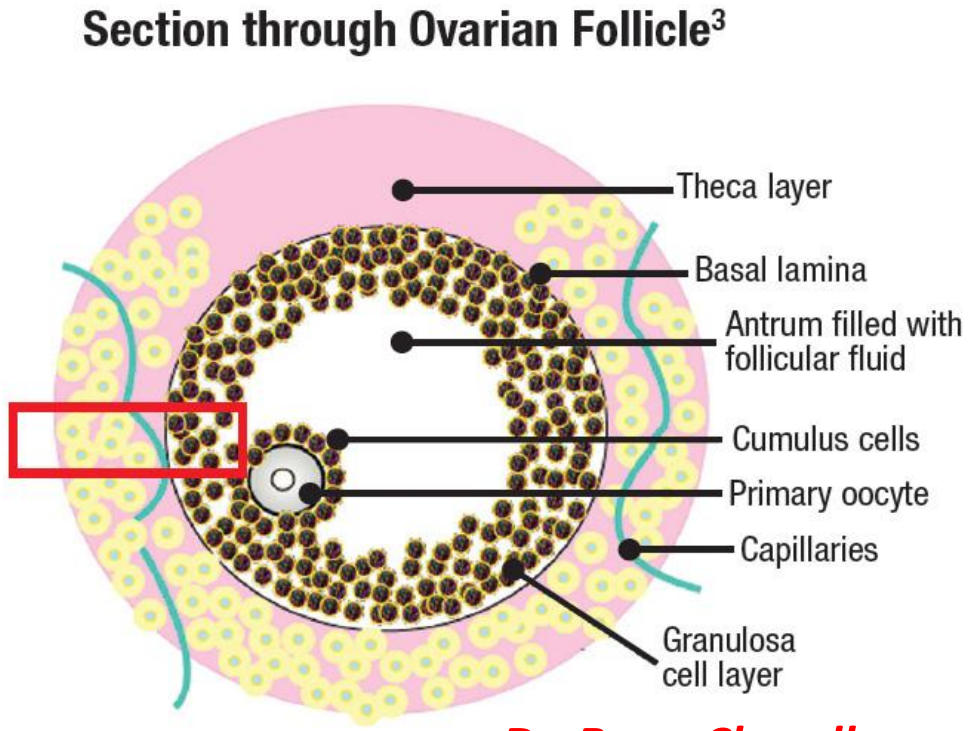

Fig. 1: AMH production

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Reshef Tal et al. Ovarian reserve testing: a user's guide. AJOG. August **2017**

Conclusion & Recommendations

- Do not use : Ovarian volume, ovarian blood flow, inhibin B, oestradiol (E2)
- Ovarian reserve curves similar to antenatal growth charts
- Can help identify patients who will have poor response / hyper response to OI for ART
- Individualize treatment protocols - Optimal response & Minimizing safety risks
- Reproductive lifespan & menopausal timing
- Aid in counseling & treatment strategy planning - Young female cancer patients
- Currently no perfect ovarian reserve test
- **AFC & AMH - Good predictive value**

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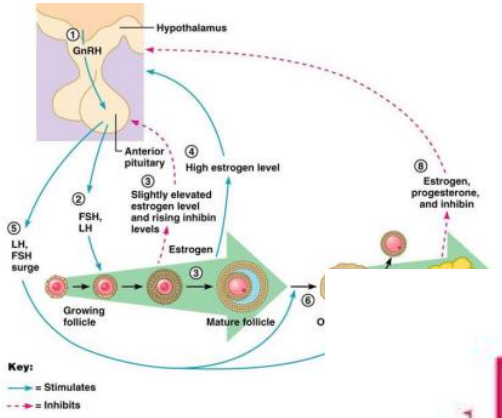
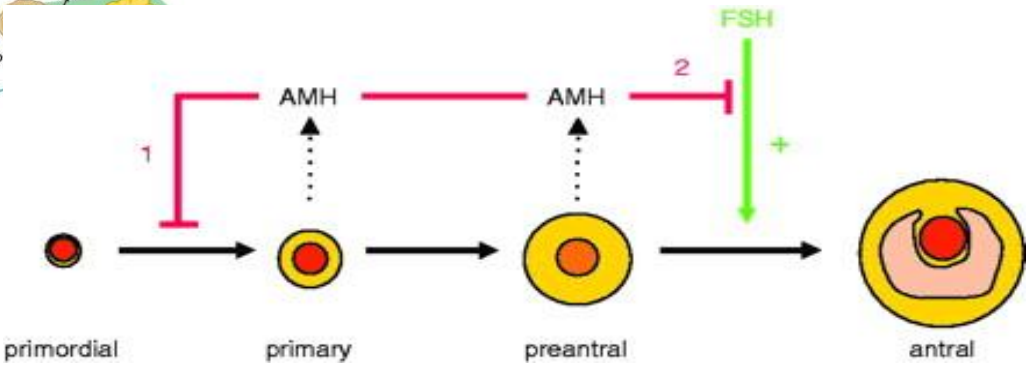
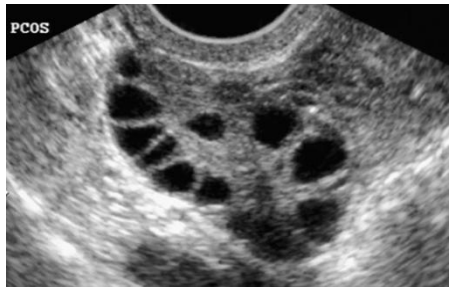
Fertility problems: Assessment and treatment. **NICE Reference Clinical guideline [CG156].** Feb 2013. Last updated: Sept **2017**

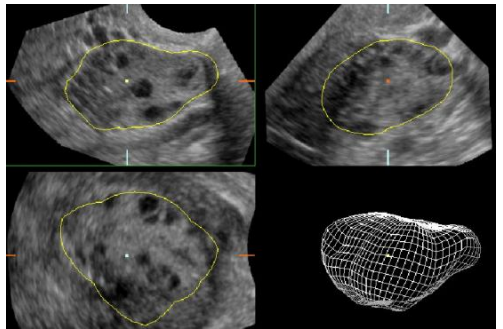
Which tests are best in PCOS?

- FSH
- AMH ✔
- AFC ✔
- Ovarian Volume









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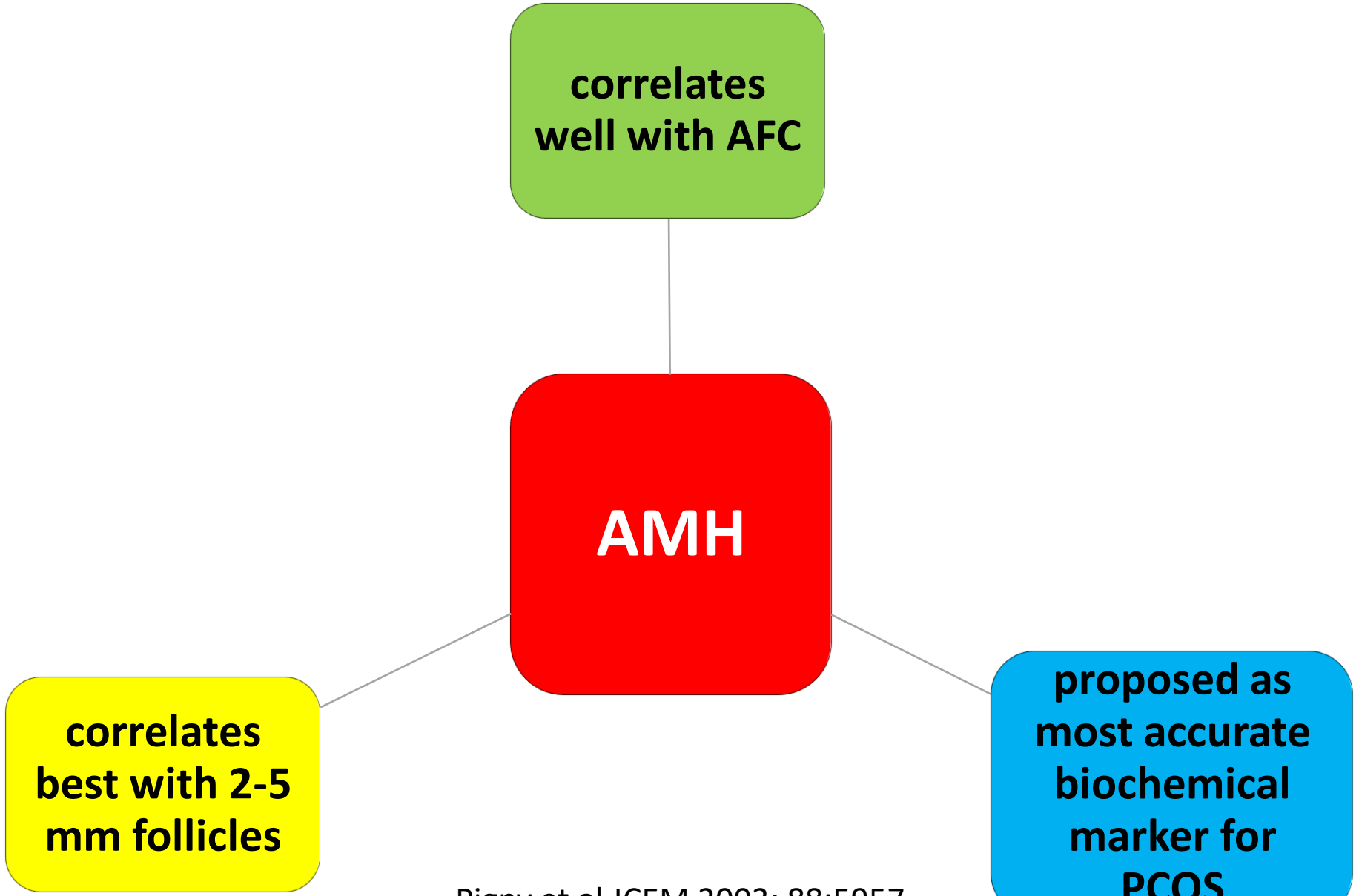

Pigny et al JCEM 2003; 88:5957
Laven et al JCEM 2004; 89:318
Dewailly et al JCEM 2010; Hum Rep 2011

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Diagnosis of PCOS

- Rotterdam consensus meeting (2003 - ESHRE/ASRM)
- Presence of at least two of three criteria with exclusion of other causes of menstrual cycle disturbance or androgen excess

✓Oligo-ovulation and/or anovulation,

✓Hyperandrogenism (clinical and/or biochemical)

✓Polycystic ovaries on USG

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Fertility problems: Assessment and treatment. **NICE Reference Clinical guideline [CG156].** Feb 2013. Last updated: Sept **2017**

AFC in PCOS

- Ultrasound criteria - Significant operator & Instrument variability
- 12 or more follicles, 2–9 mm in diameter in follicular phase & Ovarian volume >10 cm^3
- Follicle number per ovary (FNPO) = 18 (>8 MHz ultrasound probes)
- **International PCOS Guidelines 2018 - FNPO ≥20 &/or ovarian volume ≥10 ml**
- Asian PCOS women have a lower FNPO

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Mahajan N et al. Establishing an Anti-Müllerian hormone cutoff for diagnosis of polycystic ovarian syndrome in women of reproductive age-bearing Indian ethnicity using automated AMH assay. J Hum Reprod Sci. **June 2019**

AMH in PCOS

AMH - surrogate marker for PCOM instead of AFC

- > 30 years - AMH better predictor than FNPO
- AMH 2–3-folds higher than in non-PCOS healthy women

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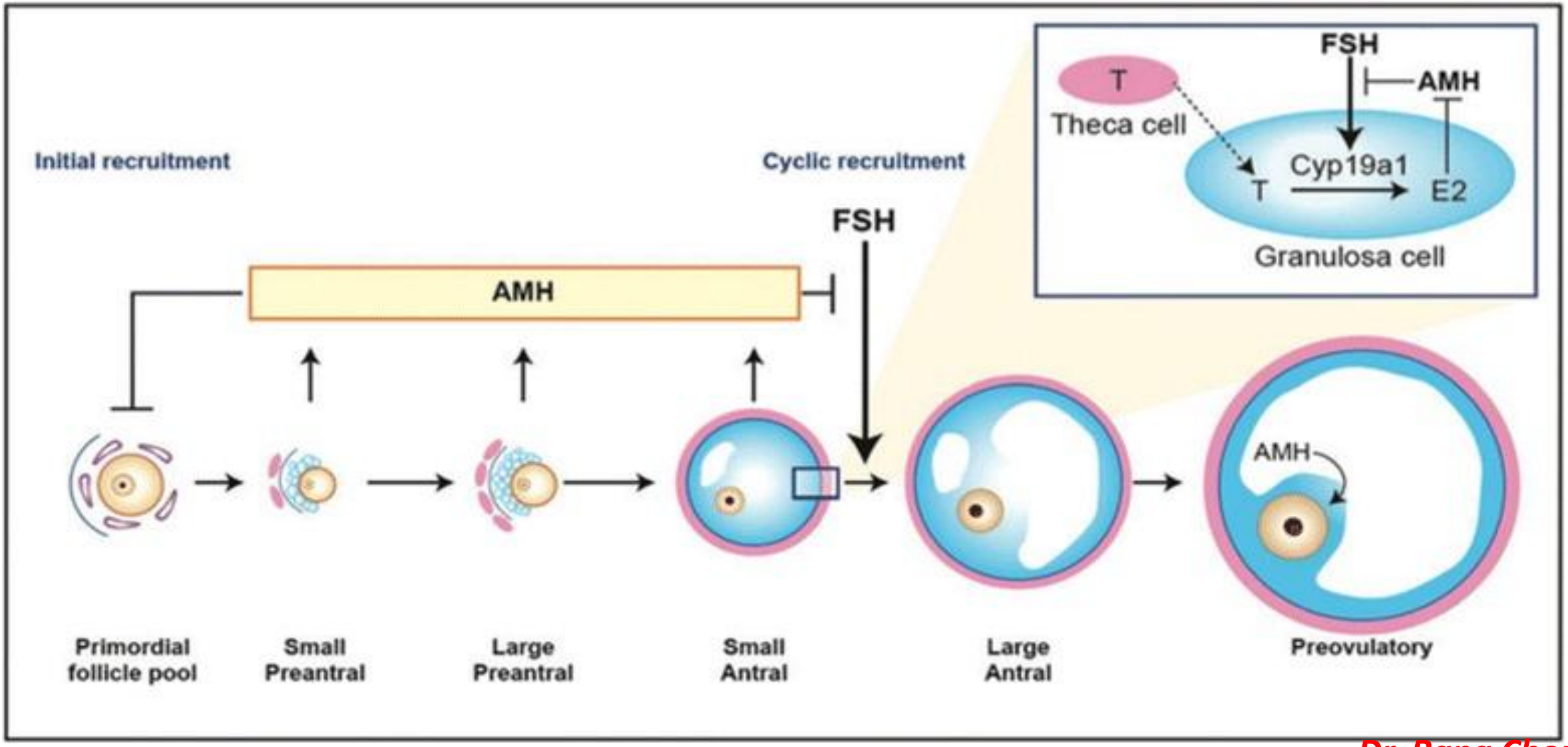
What regulates entry of follicles into growing pool



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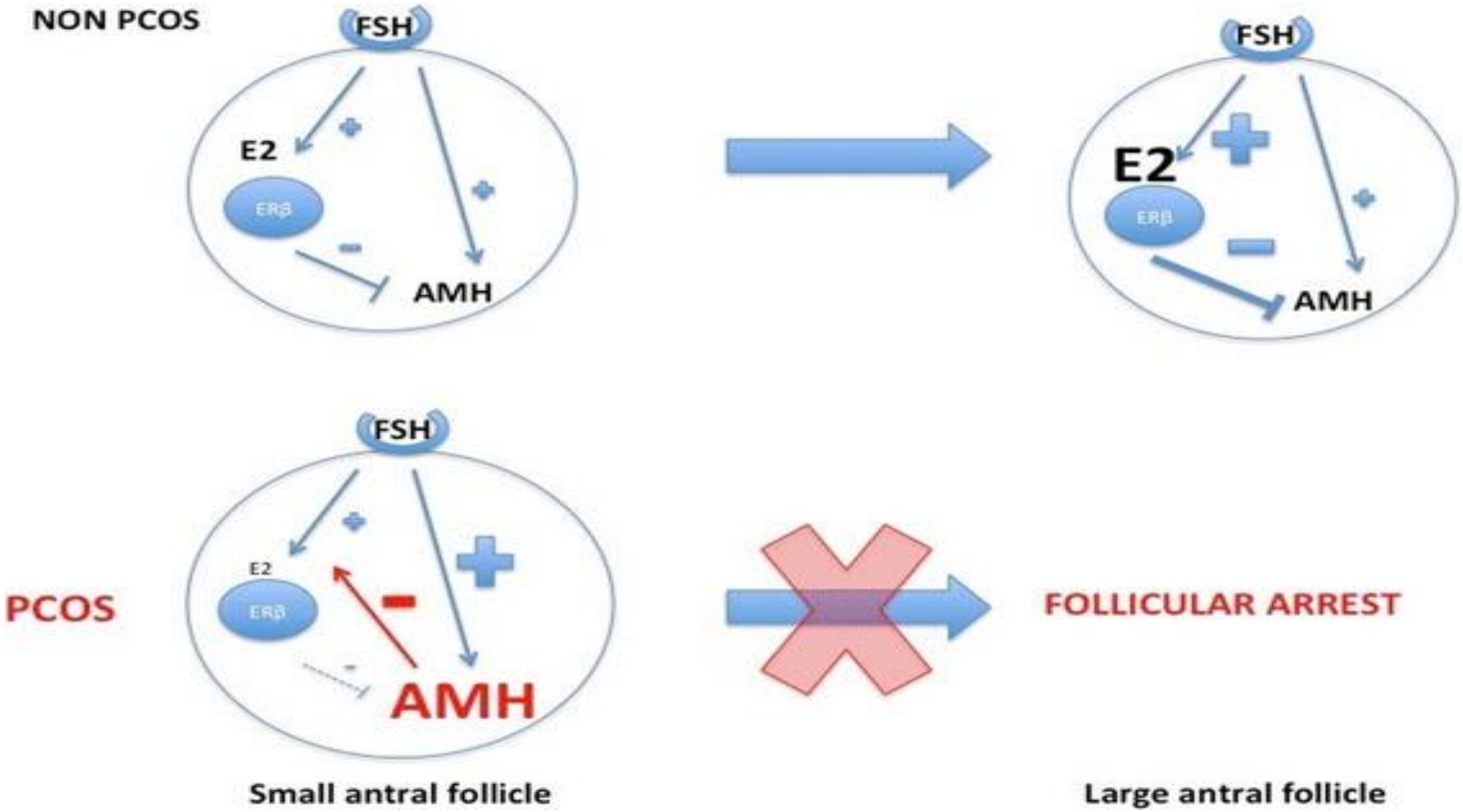
Dumont et al. Role of AMH in pathophysiology, diagnosis & treatment of PCOS: a review. Reproductive Biology and Endocrinology. **2015**



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Dumont et al. Role of AMH in pathophysiology, diagnosis & treatment of PCOS: a review. Reproductive Biology & Endocrinology. **2015**

Optimum cut off values for AMH in PCOS

- AMH levels in women with PCOS (phenotype A) was significantly higher than the other phenotypes
- Phenotype A - Highest risk of OHSS
- Caucasian population : AMH 3.5 ng/ml to 8.4 ng/ml

Author	Ethnicity	Year	AMH assay	AMH cut off (ng/ml)	AUC	Sensitivity (%)	Specificity (%)
Pigny *et al.*	Caucasian	2006	IOT	8.4	0.851	67	92
Hart *et al.*	Caucasian/Australia	2010	IOT	4.2	0.641	53.1	69.8
Dewailly *et al*	Caucasian	2011	IOT	4.9	0.973	92	97
Homburg *et al*	Caucasian	2013	DSL	6.72	0.81	60.0	98.2
Casadei *et al.*	Caucasian/Italy	2013	IOT	4.62	0.97	95.0	95.0
Sahmay *et al*	Caucasian/Nordic	2013	DSL	3.94	0.92	80.0	89.8
Fong *et al*	Caucasian	2017	Gen II	5.5(young women <30 yrs) 5(old women >30 yrs)	0.903(young women) 0.948(old women)	82	84.1
Tremellen *et al.*	Austarlia/Caucasian	2015	Elecys automated	5.07	0.836	83.7	82.3
Pigny *et al*	Caucasian	2016	Automated	4.2	0.93	-	92
			Manual	5.6			
Iliodromiti *et al*	Metaanalysis	2013	IOT	4.7	0.87	82.8	79.4

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Mahajan N et al. Establishing an Anti-Müllerian hormone cutoff for diagnosis of polycystic ovarian syndrome in women of reproductive age-bearing Indian ethnicity using automated AMH assay. J Hum Reprod Sci. **June 2019**

Optimum cut off values for AMH in PCOS

- Ethnic & racial differences in ovarian reserve
- Indian ethnicity - AMH > 5.03 ng/mL (sensitivity 70.68% & specificity 79.91%)
- A much higher threshold value, however, has been given by other Asian groups

Author	Ethnicity	Year	AMH assay	AMH cut off (ng/ml)	AUC	Sensitivity (%)	Specificity (%)
Lin *et al*	Taiwan	2011	DSL	7.3	0.774	76	70
Chao *et al*.	Taiwan	2012	DSL	3.5	-	74.0	79.0
Woo *et al*	Korea	2012	IOT	7.82	0.86	75.9	86.8
Wiveko Budi *et al*	Iran	2014	Gen II	4.45	0.87	76	74.6
Song *et al*	Korea	2017	GEN II	10	0.876	71	93
Chao-Yan *et al*	Chinese	2018	Union	8.16 (20-29)	0.85	78.4	80.9
			Immunanalyser	5.89 (30-39)	0.86	82.6	79.8
Matsuzaki	Japan	2017	Elecsys	10	-	24.6	92.6
Mahajan & Jasneet	INDIA	2018	Elecsys	5.03	0.826	70.68	79.91

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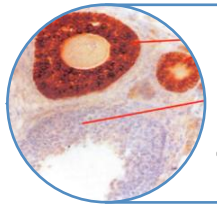
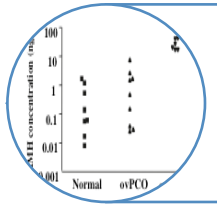
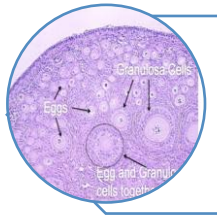
Are AMH levels different in PCOS?



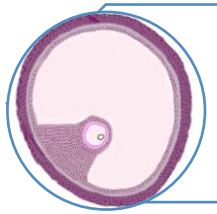
AMH per granulosa cell was compared between normal ovaries, ovulatory & anovulatory PCOs (Laura Pellatt et al J Clin Endocrinol Metab 92: 240 –245, 2007)



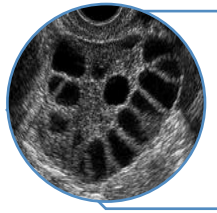
AMH production was on average 75 times higher per granulosa cell from anovulatory PCOS & 20 times from ovulatory PCOS than healthy ovaries



↑AMH – Intrinsic property of granulosa cells in PCOS, persists even after stimulation for IVF (Catteau-Jonard et al., 2008)



↑AMH concentrations are also found in follicular fluid (Das et al., 2008)



Anovulatory PCOS have 18 times higher AMH than women with ovulatory PCOS (Pellatt et al., 2010)

Facts about AMH levels in PCOS

Cut-off values of AMH have been proposed - Varying sensitivity & specificity (Pigny et al., 2006; Lin et al., 2011)

Elevated AMH - 91.7% specificity & 79.4% sensitivity in predicting amenorrhoea when AMH was 11.4 ng/ml (Tal et al., 2014)

Higher AMH in PCOS patients with IR in comparison to PCOS without IR (Fonseca et al., 2014)

Positive correlation – AMH, HOMA-IR & Insulin levels

Negative correlation - AMH & HOMA-B in both groups

Relationship between AMH & IR is in- dependent of PCOS status (Nardo et al., 2009; Skalba et al. 2011)

AMH has been shown to be negatively correlated with BMI (Fleming et al., 2015)

AMH & AFC in PCOS

- Lower rate of AMH fall increases their fertility window
- Increase in no. of recruitable follicles at an advanced age allows better ART outcomes
- Poor oocyte quality - Heterogeneity of steroidogenesis between individual follicles, altered intrafollicular environment, ↑ granulosa cell apoptosis, impaired mitochondrial function due to oxidative stress & epigenetic modification

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Correlation between AMH & AFC

Positive correlation between AMH & AFC ($P < 0.0001$) (Pigny et al., 2003)

AMH is tightly correlated with the 2 – 5 mm but not 6 – 9 mm follicular number (Pigny et al., 2003)

AMH levels are increased & tend to be associated with LH levels in PCOS (Piouka A et al 2010)

AMH had negative correlation with FSH concentration ($P < 0.04$) *(Pigny et al., 2003)*

Did not correlate with serum FSH levels (Piouka A et al 2010)

AMH & AFC in PCOS - Conclusion

- Sr AMH > 5.03 ng/mL done on automated assay (Indian origin)
- AMH - Differentiate between PCOS phenotypes
- PCOS & polycystic ovarian morphology (PCOM) - Higher response to gonadotropin & higher total no. of mature oocytes

Serum AMH is likely to emerge as an important marker of PCOS

May replace PCOM in diagnostic criteria for women of reproductive age group

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Mahajan N et al. Establishing an AMH cutoff for diagnosis of PCOS in women of reproductive age-bearing Indian ethnicity using automated AMH assay. J Hum Reprod Sci. **June 2019**

Recommendations - PCOS

- AMH should not yet be used as an alternative for detection of PCOM / PCOS (EBR)
- With improved standardisation of assays & established cut off levels (large scale validation) - AMH may become more accurate in detection of PCOM (CPP)
- Indian PCOS – Higher infertility & Lower live birth rates following IVF (CCP)

1. Helena Teede et al. International evidence based guideline for the assessment & management of PCOS **2018** (CREPOS, Monash University, ASRM, ESHRE)
2. Malik, et al.: Management of PCOS in India. A Consensus Evidence-based Good Clinical Practice Recommendations. April **2015**
3. Mehta J, Kamdar V, Dumesic D. Phenotypic expression of polycystic ovary syndrome in South Asian women. Obstet. Gynecol. Surv. **2013**

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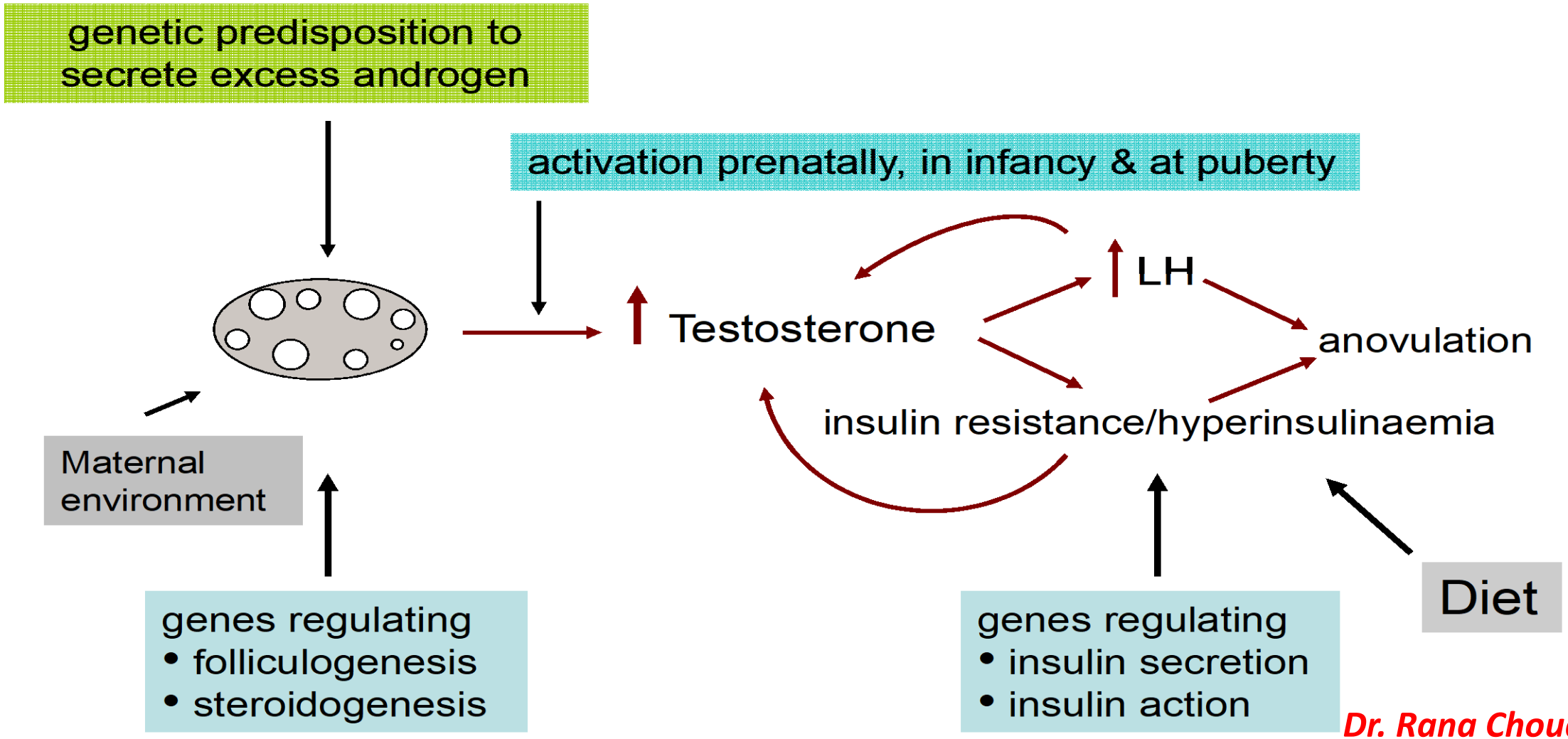
Any association between candidate gene in PCOS & Ovarian response?



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Candidate genes in PCOS that influence ovarian response

Steroid hormone production and metabolism

- CYP11a (P450scc)
- CYP17 (P450c17)
- CYP19 (P450arom)

Metabolic: insulin secretion and action; obesity

- Beta cell function: TCF7L2, KCNJ11
- Insulin resistance: IR, PPARγ
- Obesity: FTO

Androgen action

Androgen receptor

Ovarian follicle development

Follistatin; FBN3

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Candidate genes in PCOS that influence ovarian response

"Genome-wide association study identifies susceptibility loci for PCOS on chromosome 2p16.3, 2p21 and 9q33.3"

Fat mass and obesity associated gene present on Chromosome 16 may be affected

LHGCR and FSHR are both located on 2p21
Chen et al, Nature Genetics 2011 43 55-59

FBN3 expression in human fetal ovary may be affected ***Hatzirodos et al FASEB 2011 Mar 16.***

Alterations in FBN3 expression occur in other organs or tissues such as the anterior pituitary, influencing hormonal regulation of the ovary or adipose tissue.

Markers in the region of chromosome 19p13.2 are associated with PCOS and FBN3 expression occurs in other organs

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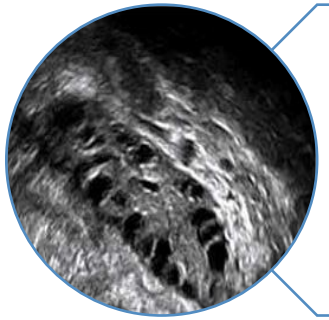
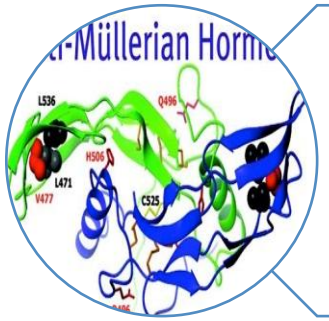
Mark J. Prodoehl; Molecular Human Reproduction, **2009**

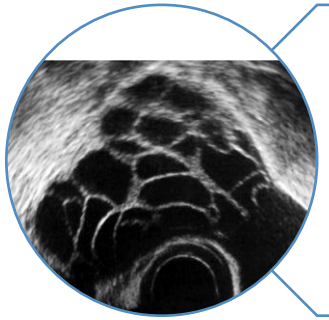
Diagnosis & Therapeutic role of AMH & AFC in PCOS



High AFC and/or serum AMH - Surrogate for oligo-anovulation / hyperandrogenism



AMH – To Establish treatment protocols, in particular to define strategy for OI in infertile oligo-anovulatory PCOS women



AMH & AFC is of value in predicting OHSS

(Broer et al., 2011a)

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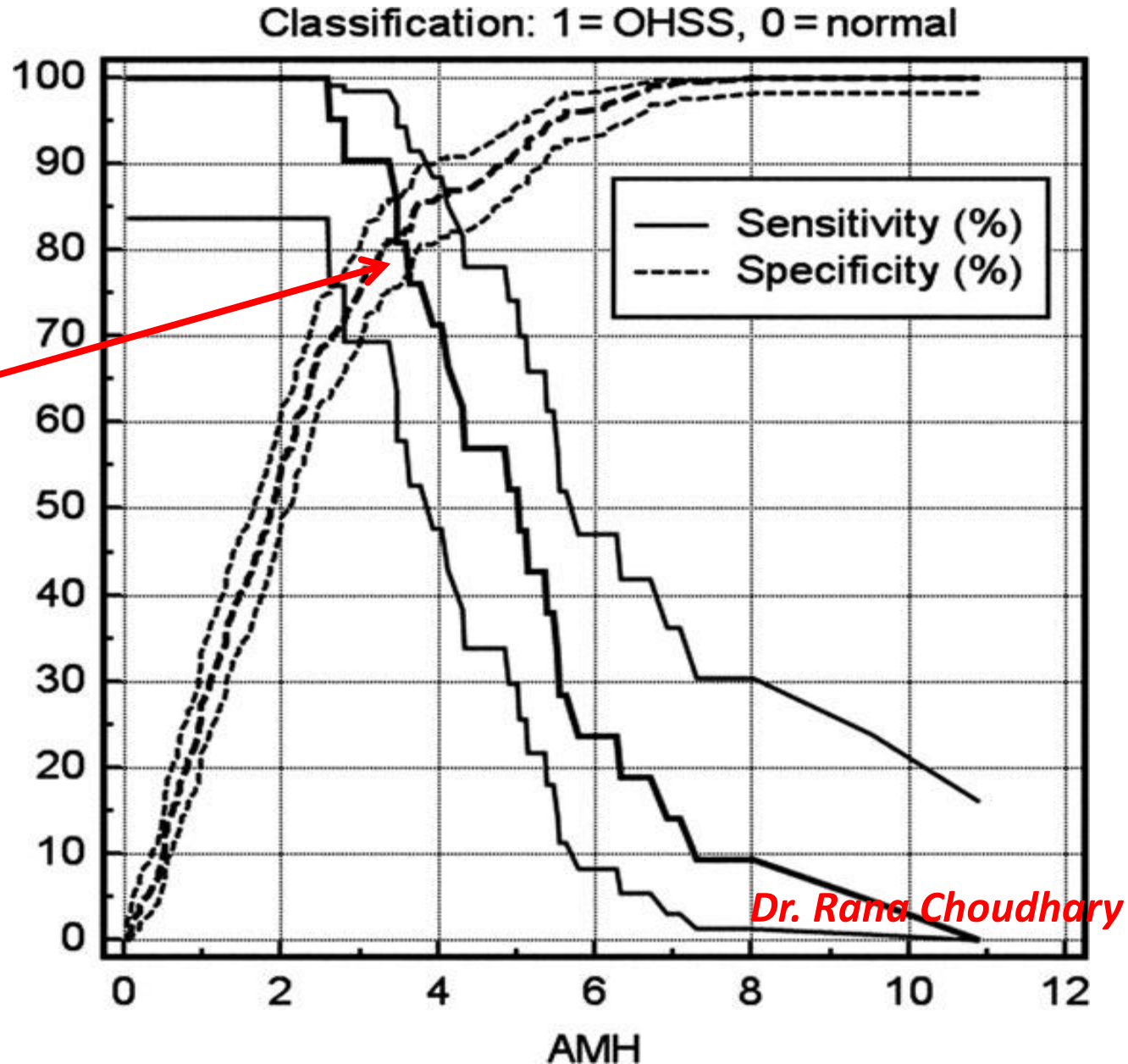
Prior level AMH predicting hyper-response

Optimal cut off 3.36 ng/ml

Sensitivity of 90.5% (95% CI 69.6–98.5)

Specificity of 81.3% (95% CI 75.8–86.0)



Lee et al HR 2008

Prior Prediction of hyperresponse (>20 oocytes) with use of AFC better: a good balance between false positive rates & sensitivity

Table 6: Sensitivity, specificity, positive predictive value (PPV) for positive test results and proportion of patients (accuracy) with a correct prediction at different cut off levels for the total antral follicle count (AFC) for the prediction of 'hyper'response in IVF.

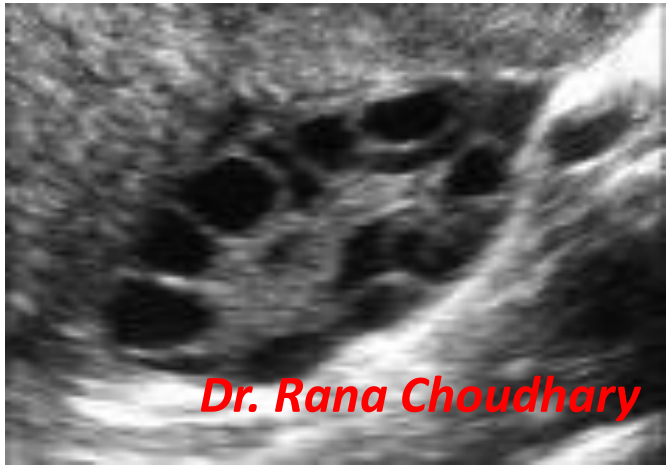
Total AFC	Sensitivity	Specificity	PPV	Accuracy
> 10	0.94	0.71	0.36	0.76
> 12	0.88	0.80	0.44	0.81
> 14	**0.82**	**0.89**	**0.58**	**0.88**
> 16	0.47	0.96	0.67	0.88
> 18	0.29	0.98	0.71	0.87

Optimum Cut off value for AFC = >14

Sensitivity 82 %

Specificity 89 %

Kwee, RBE 2007



Sensitivity, specificity, positive and negative predictive values for prediction of high ovarian response at optimum cut off levels of variables

Table 3 Comparison of performance of variables for high ovarian response by ROC curve analysis

Variable	AUC	Cutoff value	Sensitivity(%)	Specificity(%)	PPV	NPP
Age(y)	0.409(0.312–0.506)	26.5	58	30	0.39	0.72
BMI(Kg/m²)	0.468(0.362–0.574)	24.1	67	42	0.25	0.64
Basal FSH(mIU/mL)	0.385(0.294–0.475)	5.05	51	36	0.37	0.72
Basal E2(pg/mL)	0.474(0.377–0.572)	43.5	69	33	0.31	0.68
AMH(pmol/l)	0.922(0.876–0.968)	34.5	93	78	0.65	0.96
Small AFC(n)	0.961(0.933–0.989)	16	89	92	0.83	0.94

PPV positive predictive value, *NPP* negative predictive value

Sensitivity and specificity for prediction of high ovarian response were 89 % and 92 % for small AFC and 93% and 78% for AMH at the cut off values of ≥ 16 and ≥ 34.5 pmol/l, (4.86 ng/ml) respectively

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J Assist Reprod Genet **(2009)**

Predicting Response & LBR with AMH levels

Ovulation & PRs were significantly higher with CC (97% $P < 0.001$, 46% $P = 0.034$) in patients with low AMH (<3.4 ng/ml) vs AMH 3.4 ng/ml or greater (48% & 19%)

(Mahran et al., 2013)

AMH was a weak predictor of live birth outcome in patients following IVF

(Iliodromiti et al., 2014)

Day 3 AMH ≥3.2 ng/ml was a predictor of IR (72.1% sensitivity, 72.7% specificity) & CPR (75.6% sensitivity, 77.3% specificity)

(Kaya et al., 2010)

AMH - 7.7 ng/ml was predictive of ovulation following LOD (78% sensitivity & 76% specificity)

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(Amer et al., 2009)

Ovarian Reserve Test & Predicting Response to COS

Tests	Low response	High Response
AFC	< / = 4	> 16
AMH	< / = 5.4 pmol/l	> / = 25.0 pmol/l
FSH	> 8.9 IU/l	< 4 IU/l

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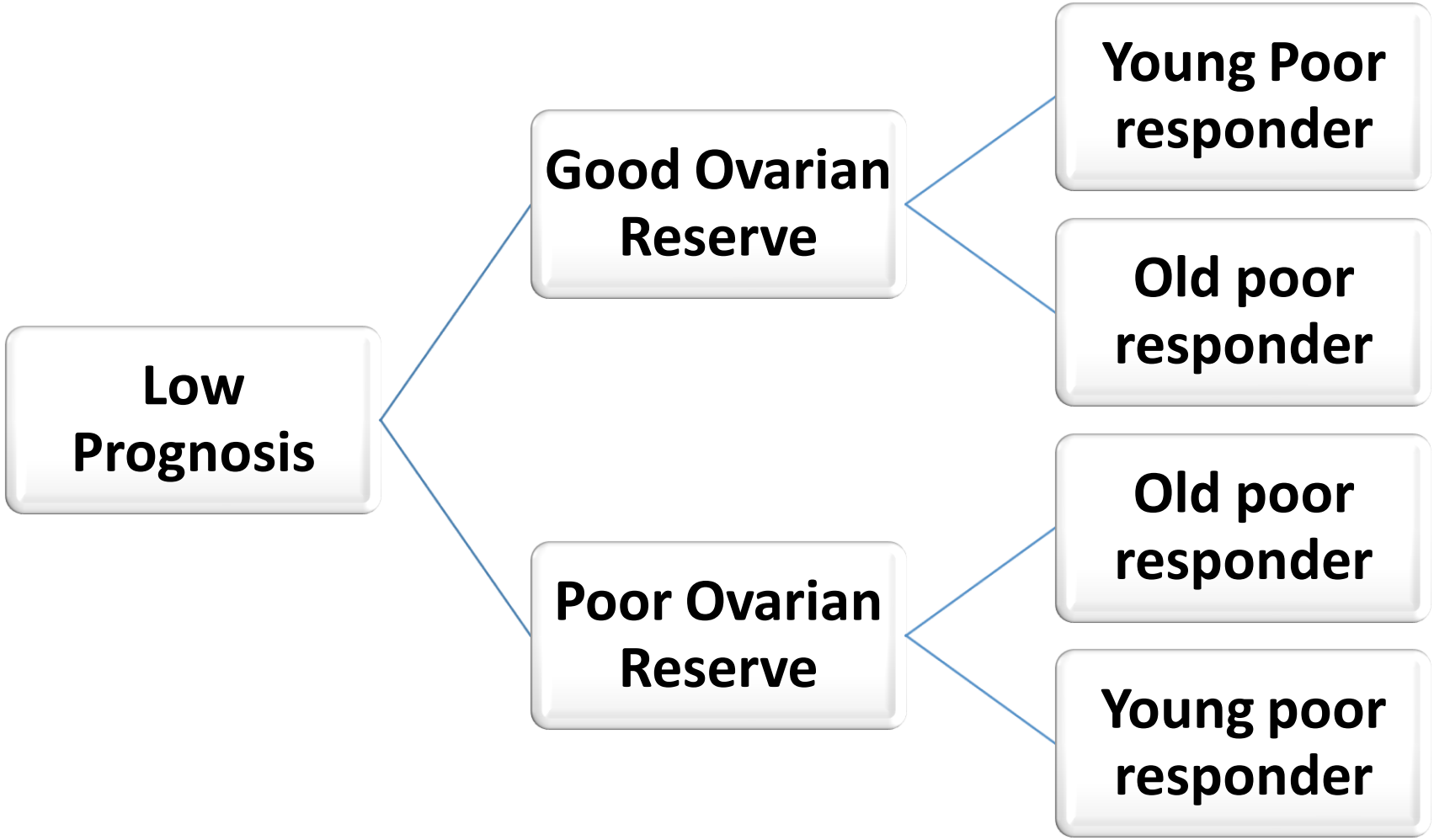
Fertility problems: Assessment and treatment. **NICE Reference Clinical guideline [CG156].** Feb 2013. Last updated: Sept **2017**
Assessing & managing ovulation disorders. **NICE** Pathway last updated: April **2018**

POSEIDON Group Labelled Patients with POR as Low Prognosis Group

POR must be categorized by age & ovarian reserve



PCOS despite having increased AFC can be poor responders

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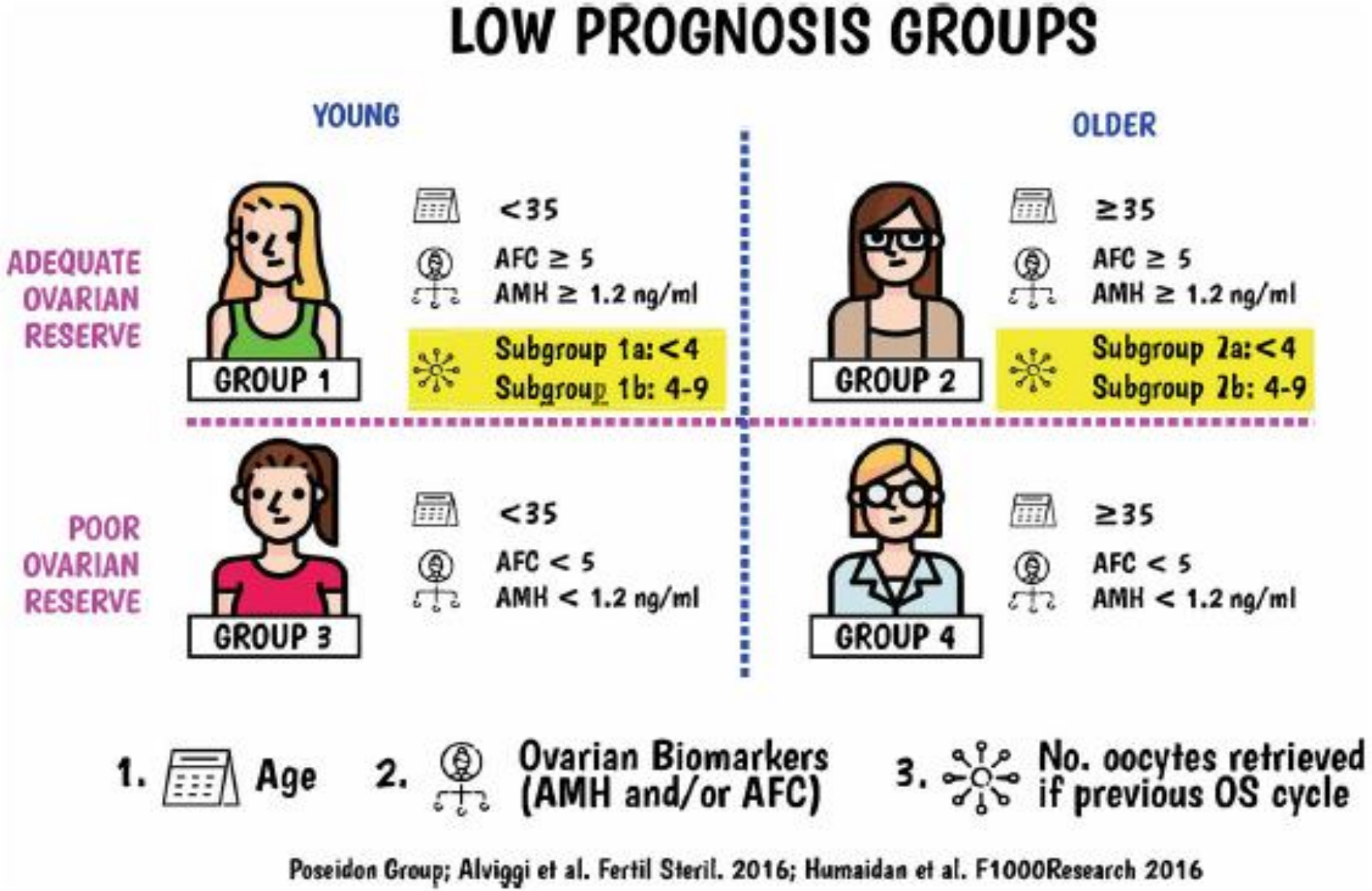

Ability to retrieve no. of oocytes necessary to obtain at least one euploid embryo for transfer in each patient

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POSEIDON Criteria is based on FORT

$$\frac{\text{Ratio of pre-ovulatory follicle (16–22mm in diameter) count (PFC) on hCG day} \times 100}{\text{Small antral follicle (3–8mm in diameter) count at baseline}}$$

- Ovarian sensitivity to gonadotropins differs from a patient to another
- Evaluates ovarian sensitivity to FSH
- Follicular Output Rate (FORT) - Efficient quantitative & qualitative marker of ovarian responsiveness to gonadotropins - Decision of treatment protocol, gonadotropin stimulation doses for hyporesponders

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Michael Grynberg. Understanding Follicular Output Rate (FORT) & its Implications for POSEIDON Criteria. Frontiers in Endocrinology. April **2019**

Prediction of IVF/ICSI outcome based on FORT

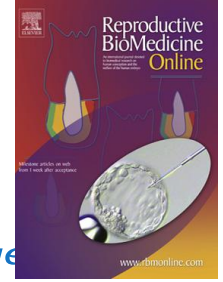

Table 4 Characteristics, ovarian stimulation data and IVF/ICSI outcomes of PCOS patients according to FORT.

	Low FORT (<0.5; n = 45)	*Medium FORT* (0.5—0.73; n = 56)	*High FORT* (>0.73; n = 39)	P-value
Age (years)	32 ± 4	32 ± 3	33 ± 4	NS
Duration of infertility (years)	5 ± 3	6 ± 3	5 ± 4	NS
Body mass index (kg/m^2)	25.72 ± 3.70	25.60 ± 3.87	24.34 ± 3.17	NS
FSH/LH ratio	1.04 ± 0.58	0.84 ± 0.53	0.82 ± 0.52	NS
Serum testosterone (ng/ml)	0.38 ± 0.16	0.37 ± 0.20	0.36 ± 0.19	NS
Serum basal oestradiol (pg/ml)	39.73 ± 19.66	39.53 ± 21.32	43.89 ± 26.38	NS
AFC	22.36 ± 5.86	19.86 ± 5.72	16.44 ± 4.94	<0.001
Dose of starting FSH (IU)	208.61 ± 59.10	228.57 ± 64.08	227.24 ± 54.33	NS
Duration of gonadotrophin (days)	10.04 ± 1.94	8.68 ± 0.96	8.64 ± 0.96	<0.001
Total gonadotrophin dose (IU)	2116.67 ± 802.68	1974.33 ± 651.38	1879.17 ± 476.65	NS
PFC	7.93 ± 2.92	11.79 ± 3.27	15.10 ± 4.89	<0.001
Retrieved oocytes	12.04 ± 7.54	15.63 ± 7.08	17.21 ± 7.66	0.005
2PN fertilization rate	63.47 (344/542)	69.49 (608/875)	60.66 (407/671)	0.001
Good-quality embryo rate	68.06 (211/310)	72.71 (373/513)	64.99 (232/357)	0.047
Implantation rate	25.51 (25/98)	31.67 (38/120)	27.59 (24/87)	NS
Clinical pregnancy rate	46.67 (21/45)	53.57 (30/56)	38.46 (15/39)	NS

- **Number of retrieved oocytes was highest in high FORT group (P < 0.05)**

- **Fertilisation Rate & good-quality were significantly higher in medium FORT group (P < 0.05)**

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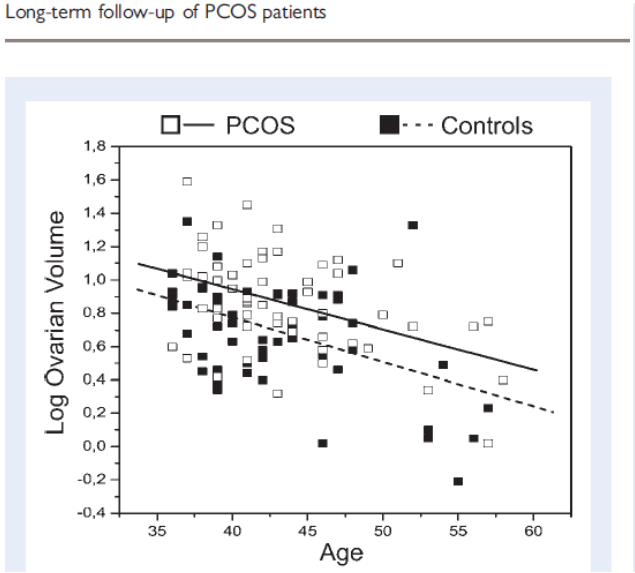
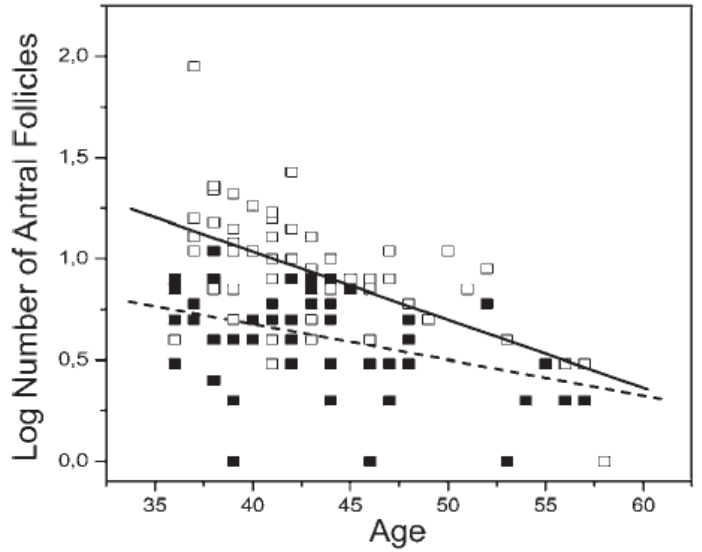
- **Better IVF/ICSI outcome was achieved in PCOS patients with medium FORT values**

Ning Zhang. RBM online **2013**

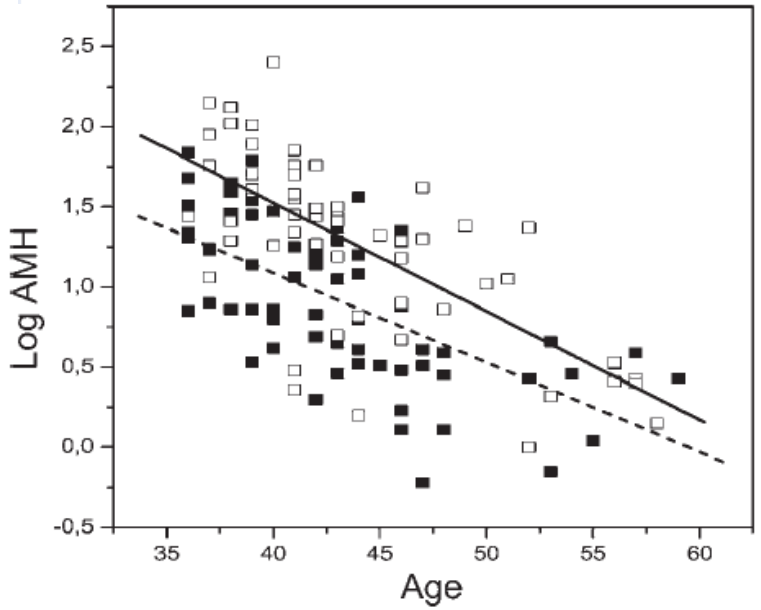
PCOS: Reproductive outcome & Ovarian reserve

- To evaluate relationship between ovarian volume, no. of antral follicles, AMH, PCOS status & Age, pre and post-menopausal PCOS patients with controls without hormonal treatment





- Ovarian reserve declined at a similar rate with age in both groups (P<0.001)
- PCOS patients had a better ovarian reserve across ages compared with controls (P<0.001 ovarian reserve variable)



M. Hudecova. Long-term follow-up of patients with PCOS: reproductive outcome & ovarian reserve. Hum Reproduction. **2009**

Conclusion

Young women with PCOS - ↑ Ovarian reserve compared with age-matched controls

Polycystic ovaries are larger & contain more antral follicles as assessed by USG

Higher levels of AMH in women with PCOS than in controls

AMH is crucial in maintaining right tempo of folliculogenesis in ovary making it one of the most important ovarian hormones & crucial factors underpinning female fertility

AMH - Best biochemical marker of ovarian function

Easy measure of submerged part of iceberg of follicle growth ('acyclic' ovarian activity)

Highly elevated AMH - Predictive of poor response to various Rx of PCOS including weight loss, OI & LOD. But do not predict LBR

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