

Predicting Recurrent Miscarriages in 2009

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FACTS

- **50%** of all pregnancies are lost, most before clinical recognition of pregnancy.
- **1%** of couples will suffer Recurrent Miscarriages, defined as **THREE CONSECUTIVE** losses. (USA 2 or more = **5%**)
- **SIGNIFICANT** psychological Trauma, vulnerable group of patients, relatively minor medical problems.

Recurrent Miscarriages

- **Recurrent Miscarriages are an independent risk factor for all Adverse Pregnancy Outcomes.**
- **The greater the number miscarriages, the less the chance of normal pregnancy.**

Recurrent Miscarriages

- **Difficult area to work in.**
- **Multifactorial, frustrating for patients and Physicians, poorly approached by busy hospitals.**
- **Most causes and treatments are not evidence based – Internet can be dangerous.**
- **Lack of logical work up = significant time wasting.**

? Investigate

- Work up needs to be consistent.
- Paternal and Maternal Age are important factors.
- Poorly Researched.
- ? Funding.
- No 'Forums' in Congresses.
- One Size does **NOT** fit all!

? Predict

- **AGE - < 35, > 35**
 - **Primary or Secondary**
 - **Embryonic (<7 weeks) or Fetal (>7) losses**
 - **Past Med, Surg, Gyn, Obstet and Family History, nutrition.**
 - **Social History, including drug use.**
- **Tests:**
 - **3 D Scan +/- Uterine Artery dopplers**
 - **AMH / Bloods**

RSA

Group I < 35

Group II 35 +

A) Primary

B) Secondary (1+/-)

A) Primary

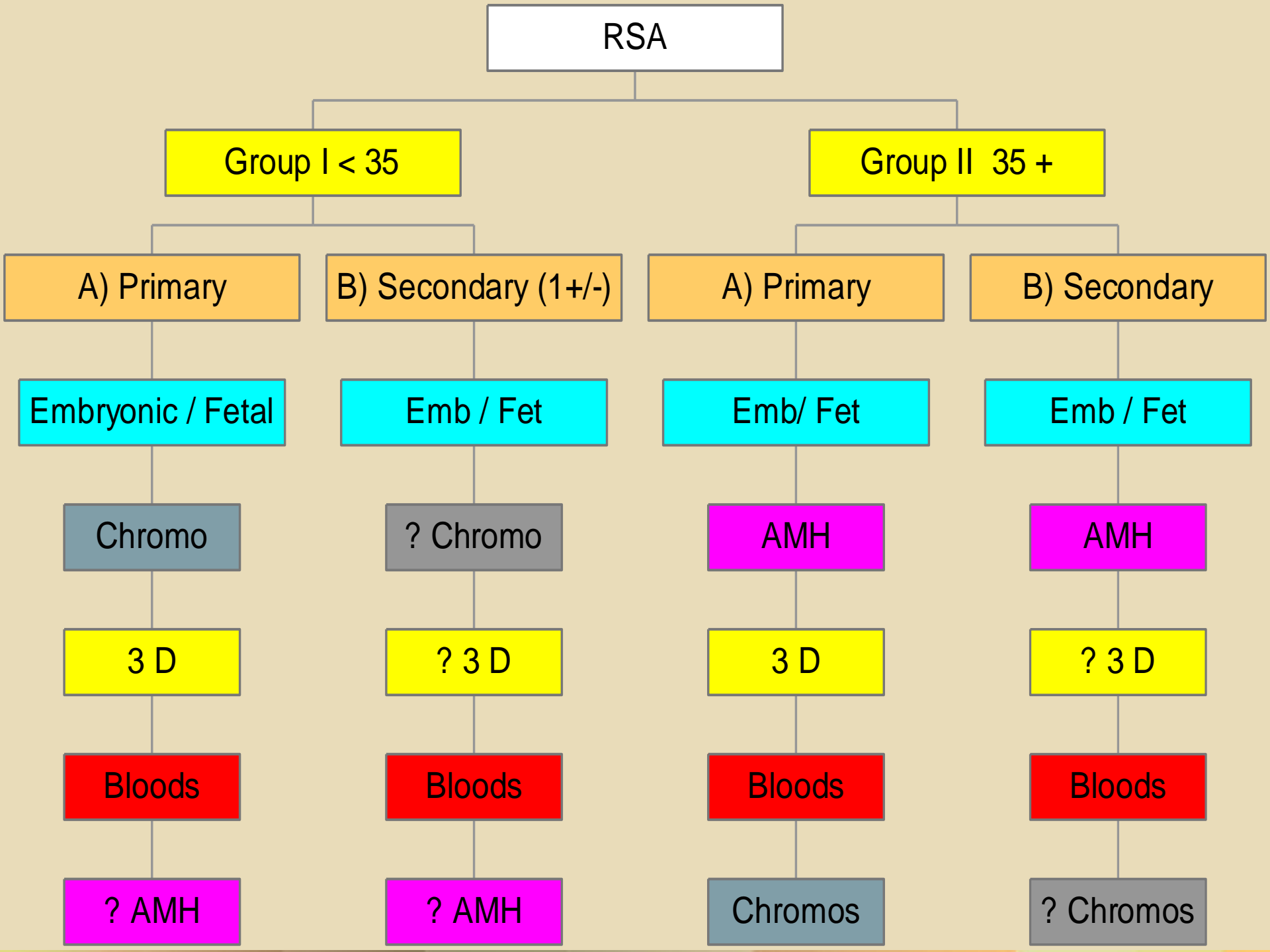
B) Secondary

Embryonic / Fetal

Emb / Fet

Emb/ Fet

Emb / Fet



RSA

Group I < 35

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A) Primary

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A) Primary

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Embryonic / Fetal

Emb / Fet

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Emb / Fet

Chromo

? Chromo

AMH

AMH

3 D

? 3 D

3 D

? 3 D

Bloods

Bloods

Bloods

Bloods

? AMH

? AMH

Chromos

? Chromos

Current Findings:

- **AGE.....!**
- **Significant Proportion of “miscarriages” are actually “Sub-Fertility”**
- **(Findings: 84% > 35 have decreased AMH's)**
- **? DNA Damage**

Anti Müllerian Hormone.

- A dimeric glycoprotein belonging to the transforming growth factor beta super family.
- A reflection of the Size and Quality of the growing pool of oocytes.

Anti Müllerian Hormone.

- **Regulates follicular development.**
- **Decreases with advancing age.**
- **Decreases precede rises in FSH, Inhibin B.**
- **Excellent marker of 'reproductive performance'.**
- **Allows realistic reproductive planning.**

LEVELS

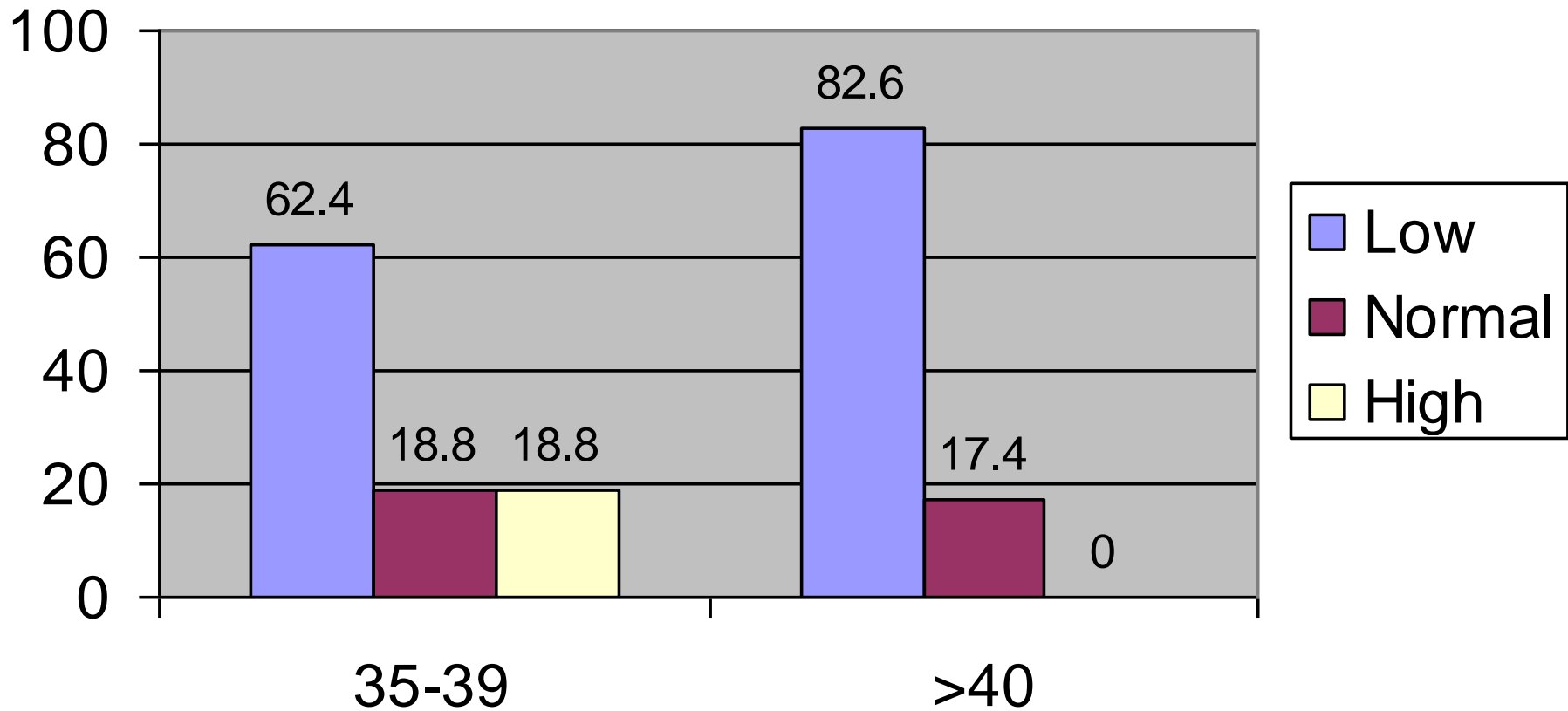
- Relatively static (20-25 pmol/L) from 18 to 29 years of age.
- By 30 years, levels decrease, reaching 10 pmol/L by 37 years.
- 50% fall in AMH levels between 29 and 37 years of age, **minimal** changes in **FSH**.
- > 30 = PCOS - Hyperstimulation

AMH

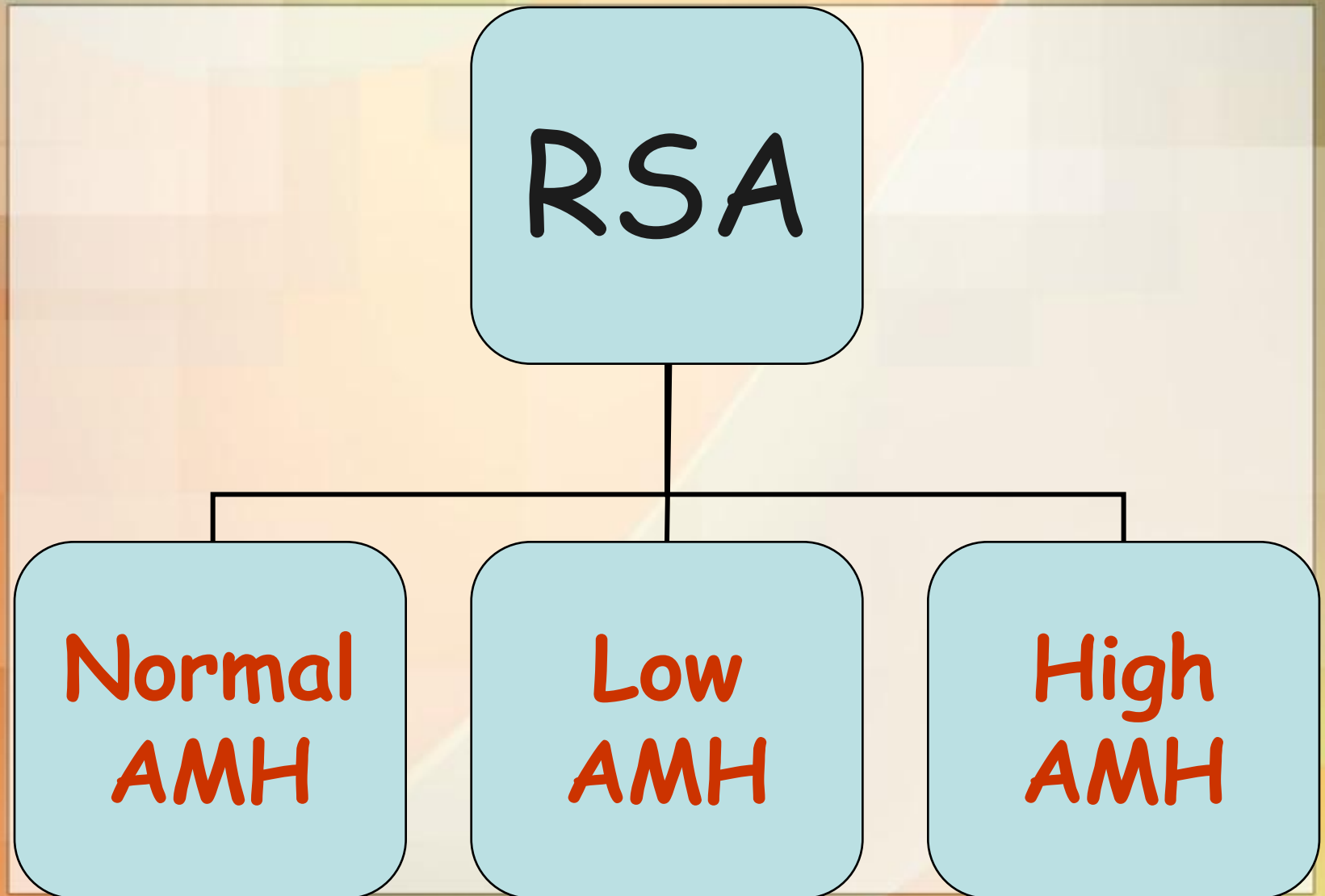
- **Serum AMH is used in infertility clinics to predict oocyte yield during ovulation stimulation.**
- **Measurement of AMH prior to IVF treatment allows clinician to give the couple a **realistic** expectation of IVF outcomes.**
- **Same in RM Clinic.**

AMH results

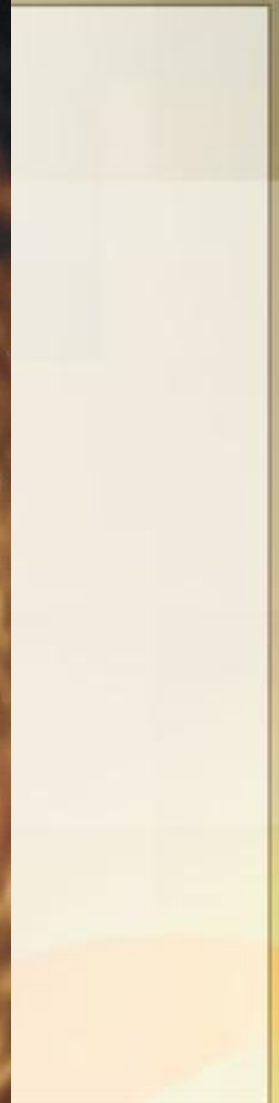
Undetectable < 3nM/L, Low < 14nM/L,
Normal 14-30nM/L, High > 30 nM/L



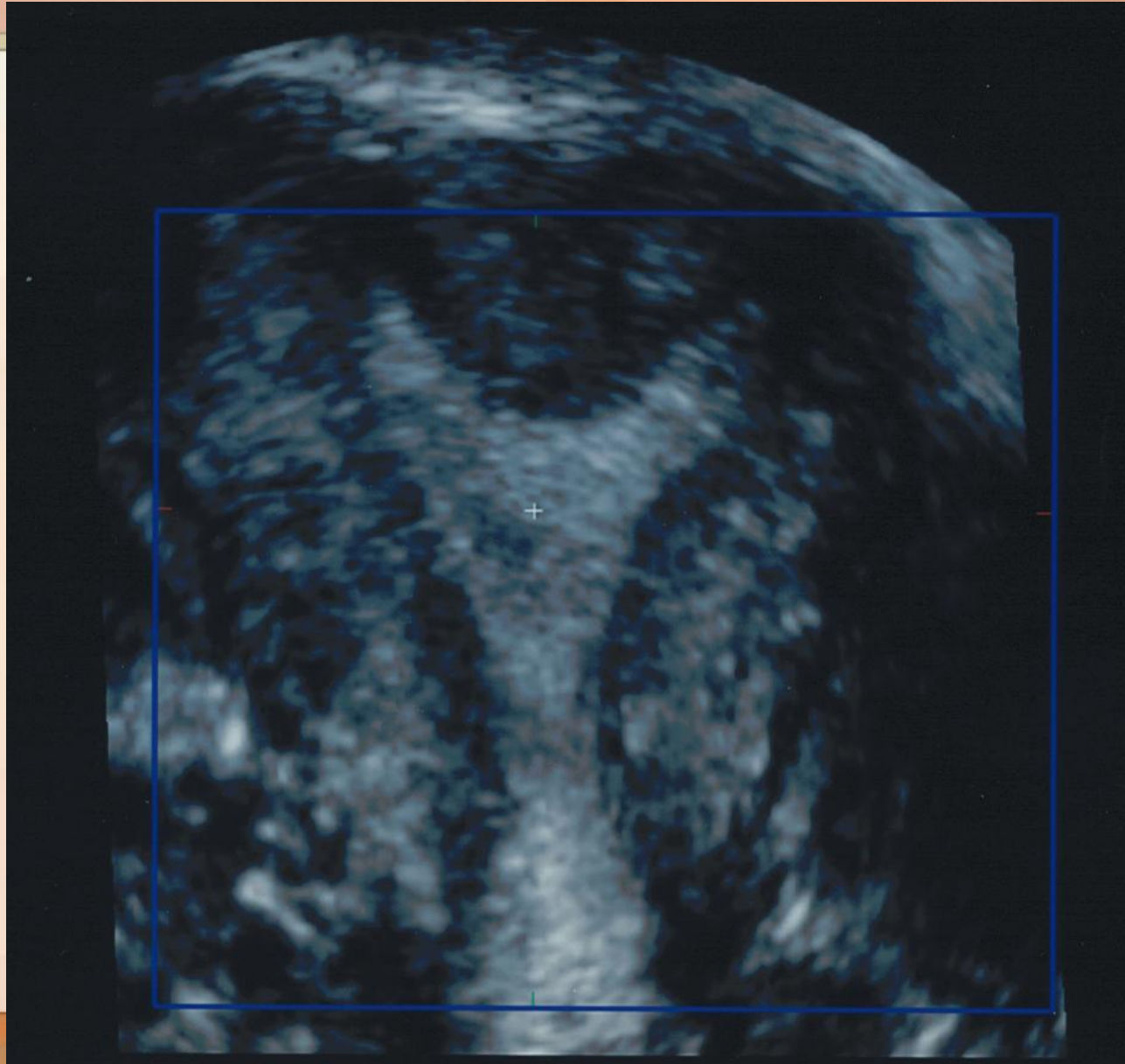
? Intervention Trials



3 D Scan



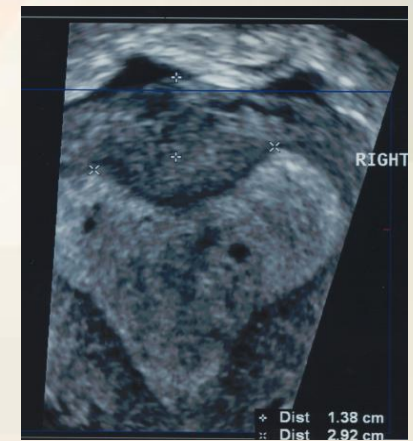
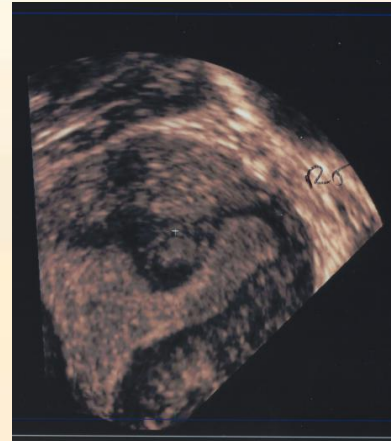
3 D Scan



3D Ultrasounds

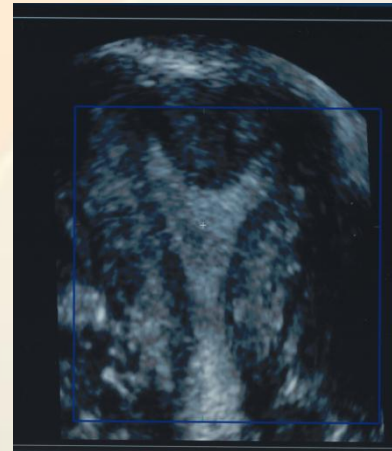
Group I A:

46% detection of congenital uterine abnormalities.



Group II A:

50% detection of fibroids or congenital uterine abnormalities.



Other findings

- **5 translocations, 4 women and 1 man.**
- **“Lifestyle Factors” – BMI Too high and too low. PCOS and Coeliac disease.**
- **Vitamin deficiencies – vegan.**
- **Hyperinsulinism and impaired GTT / Thyroid disease.**
- **Hyperhomocysteinaemia.**
- **Methadone – prolactin.**
- **SLE / UCTD / APS**
- **‘Thrombophilias’**
- **Uterine abnormalities.**

Conclusions:

- **Age and obstetric history adjusted approach lessens work up time.**
- **Detecting 'subfertility' allows appropriate counselling and referral if necessary.**
- **Decreasing AMH does not mean that pregnancy is impossible, but does impose a time limit.**

PREDICTIONS?

- **AMH**
- **3 D Scan**
- **Thrombophilic**
- **Endocrine**
- **Immune**
- **Metabolic**
- **Genetic**
- **Nutrition**
- **Compare with 'normal' Couples.**
- **Establish Prevalences specific to pregnancy and Australia.**
- **?Screening tests/ Risk assessment**

PLANS

- **Set up Databases / RCT's - "Network" other groups.**
- **Work with PAPO to recruit patients.**
- **Seek funding.**
- **RM affects 1% of the population, more research and publications needed.**

Acknowledgements:



PAPO

Predicting

Adverse

Pregnancy

Outcomes

This work is part of
a larger Study -
"PAPO"

Prediction of
Adverse Pregnancy
Outcomes

Researchers:

Dr C D McCormack

A/Prof. Claire Roberts

A/Prof Gus Dekker.

Dr. Denise Furness

Pathway in PIU Clinic

- Emergency Dept. Recurrent? - Bloods, Clinic appointment.
- 6 weeks - fasting, complete blood work up, confirm history, enroll in trial. Book ultrasound, Partner bloods ? Counselling.
- 2-3 weeks - Follow up results, ? Gynaecology ? Infertility referral, ? Physician.
- Discuss plans and meds / lifestyle changes etc.
- See when pregnant, follow up to 12 weeks +/- more if wanted.

Work Up

- Chromosomes.
- Immune: Thyroid antibodies, ANA ?ENA
- Thrombophilic Screen – genotypes (FVL, PGM, MTHFR, PAI1, AT III) and APAS, (KCT DRVVT, ACL and beta 2 glycoprotein 1 abs, activated prot C resistance)
- Metabolic: GTT + Insulin (BMI > 28)
 - Fasting homocysteine, lipid profile folate B12, red cell folate.
- Endocrine: TSH, Prolactin, FSH. LH, FAI, SHBG, Testosterone.