Ultrasonography in Management of Subfertility

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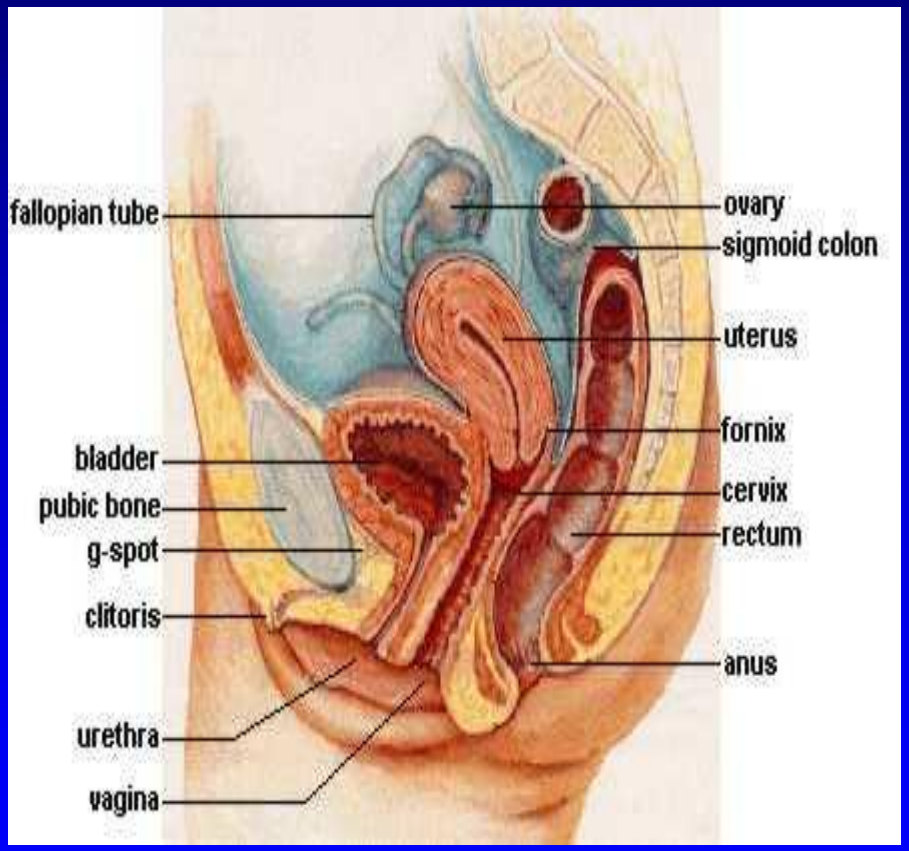
Ultrasonography in subfertility

1. Workup for subfertility
2. Assisted reproduction technique
3. Early pregnancy scanning
   - Number of gestational sacs
   - Viability
   - Ectopic pregnancy

Subfertility workup

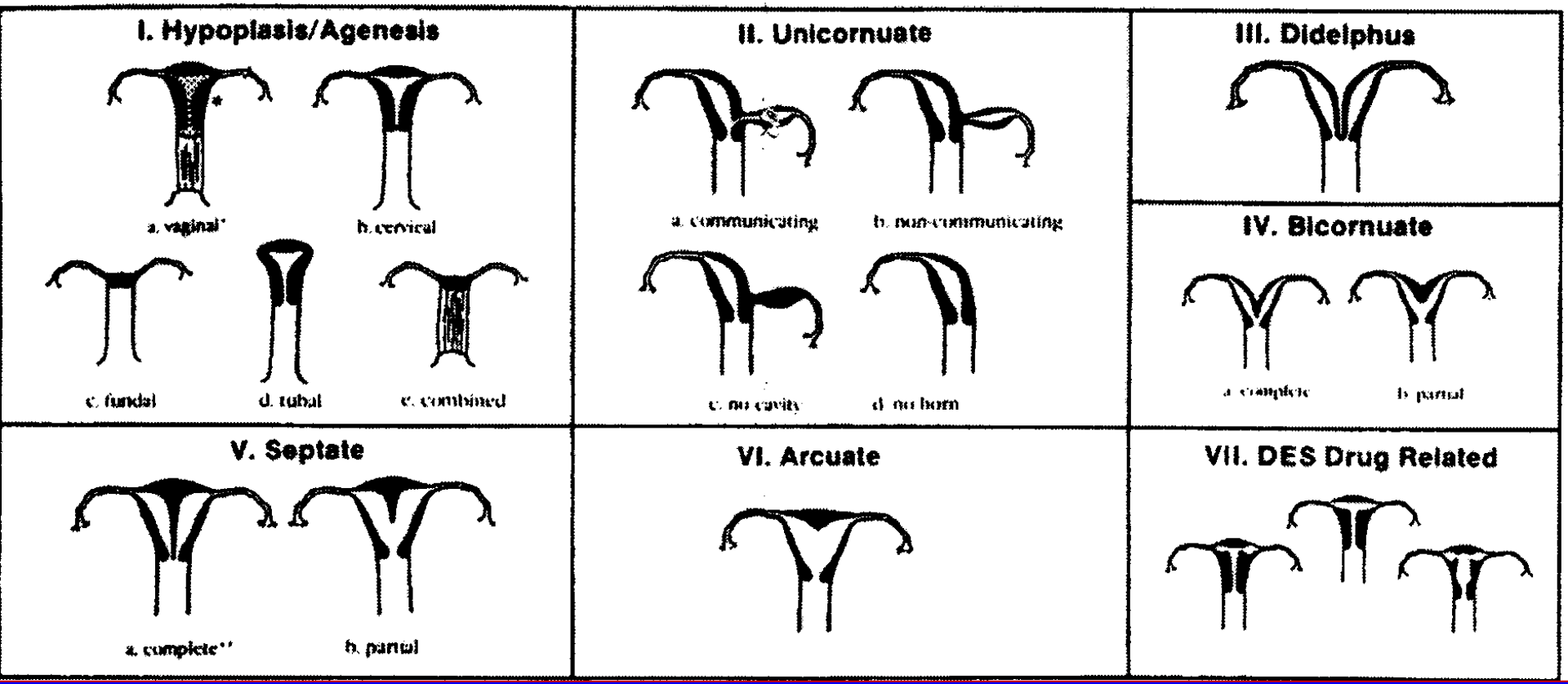


- Uterus
- Ovary
- Fallopian tubes
- Others

Uterus

1. Congenital uterine abnormalities
2. Fibroid and polyps

Congenital uterine abnormalities



ASRM classification

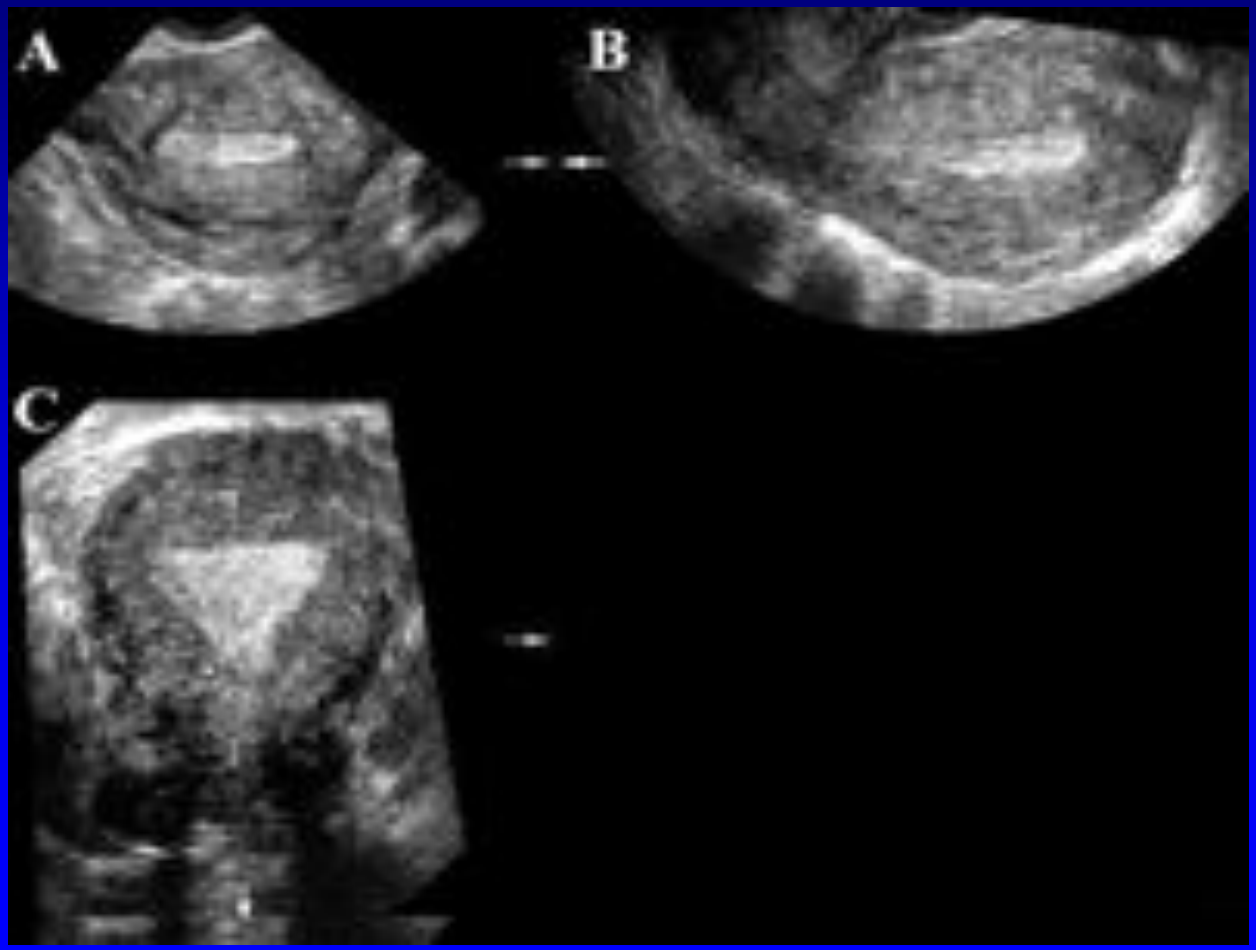
Congenital uterine abnormalities

Table 1. Classification of Congenital Uterine Anomalies*

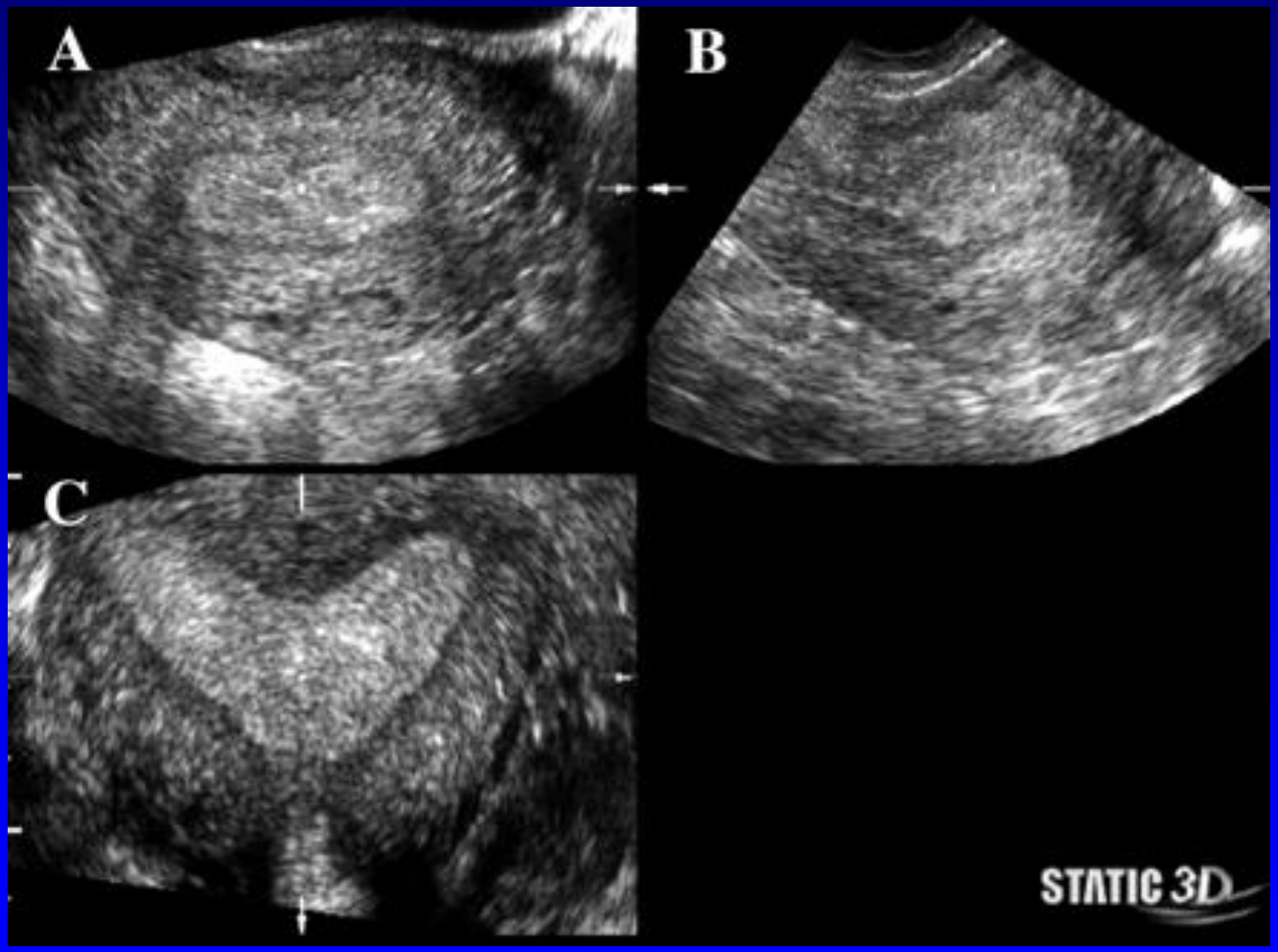
Uterine morphology	Fundal contour	External contour
Normal	Straight or convex	Uniformly convex or with indentation <10 mm
Arcuate	Concave fundal indentation with central point of indentation at obtuse angle	Uniformly convex or with indentation <10 mm
Subseptate	Presence of septum that does not extend to cervix, with central point of septum at an acute angle	Uniformly convex or with indentation <10 mm
Bicornuate	Two well-formed uterine cornua, with a convex fundal contour in each	Fundal indentation >10 mm dividing the two cornua

* Based on criteria suggested by The American Fertility Society, 1988.[5]

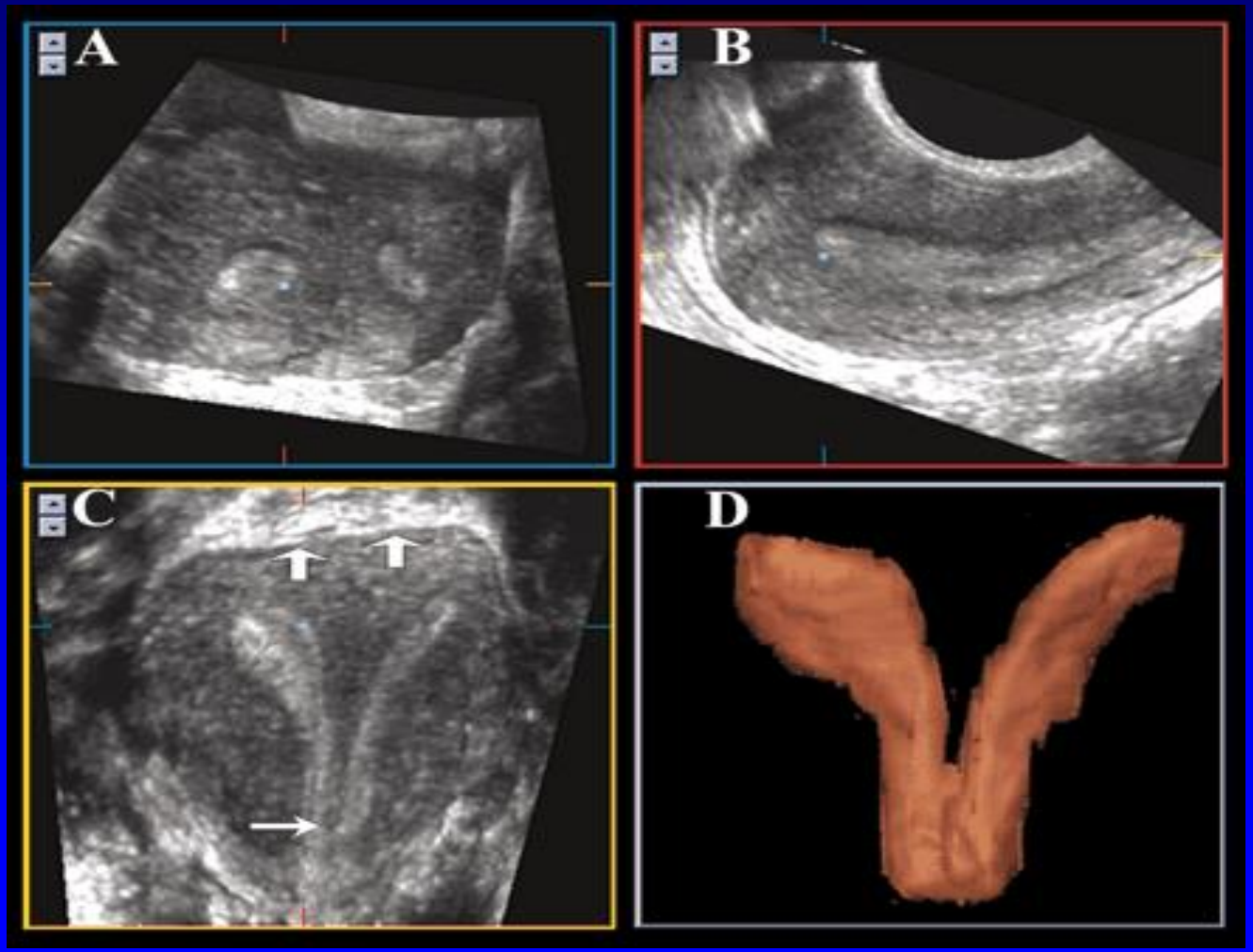
Normal uterus



Arcuate uterus



Septate uterus

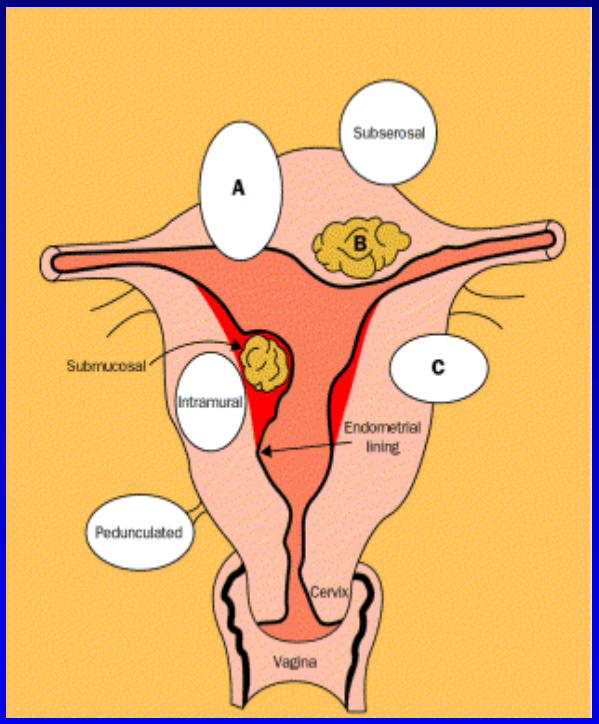


Congenital uterine anomalies

- Associated with a range of adverse reproductive outcomes
- Septate uterus had a higher proportion of 1st trimester loss compared with women with a normal uterus.
- Women with an arcuate uterus had a greater proportion of 2nd trimester loss and preterm labor.

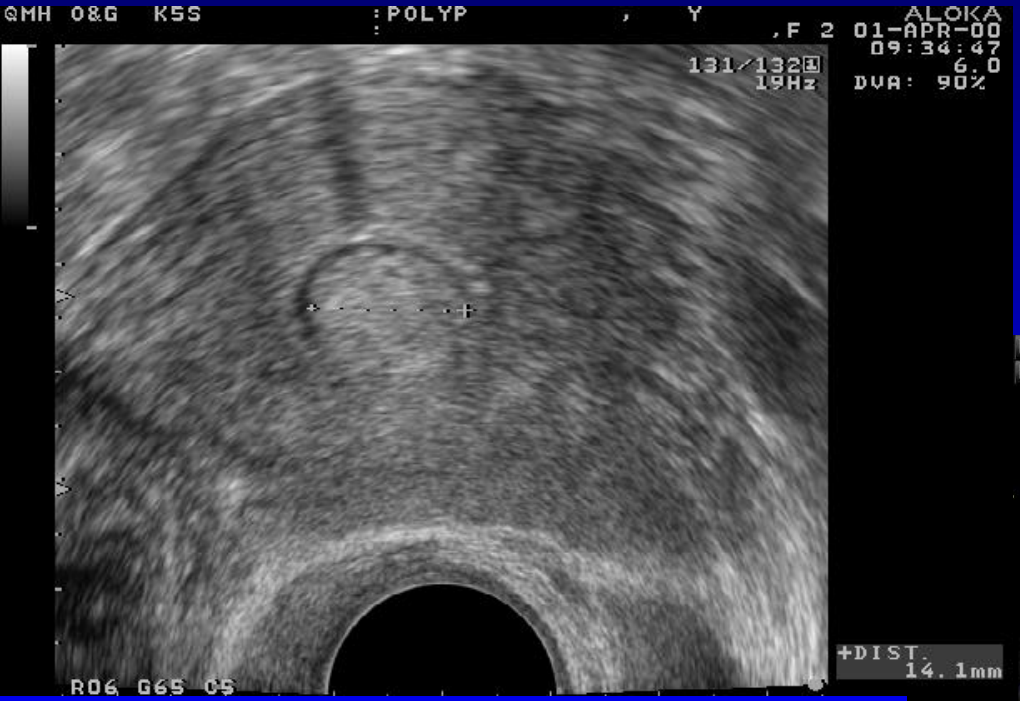
(Woelfer et al., 2001)

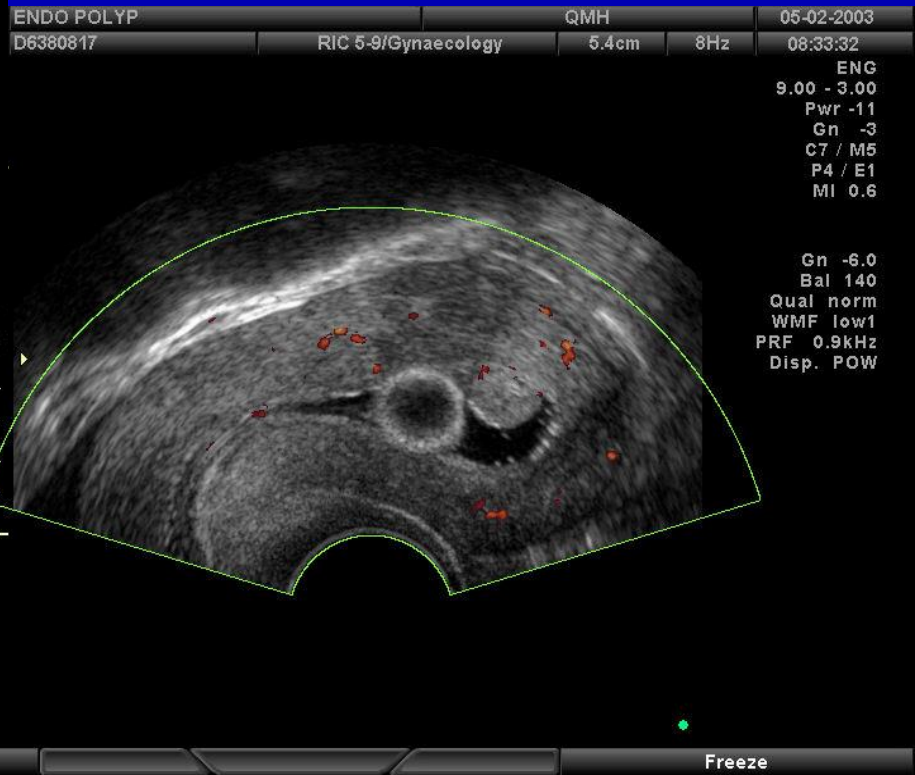
Uterine fibroids



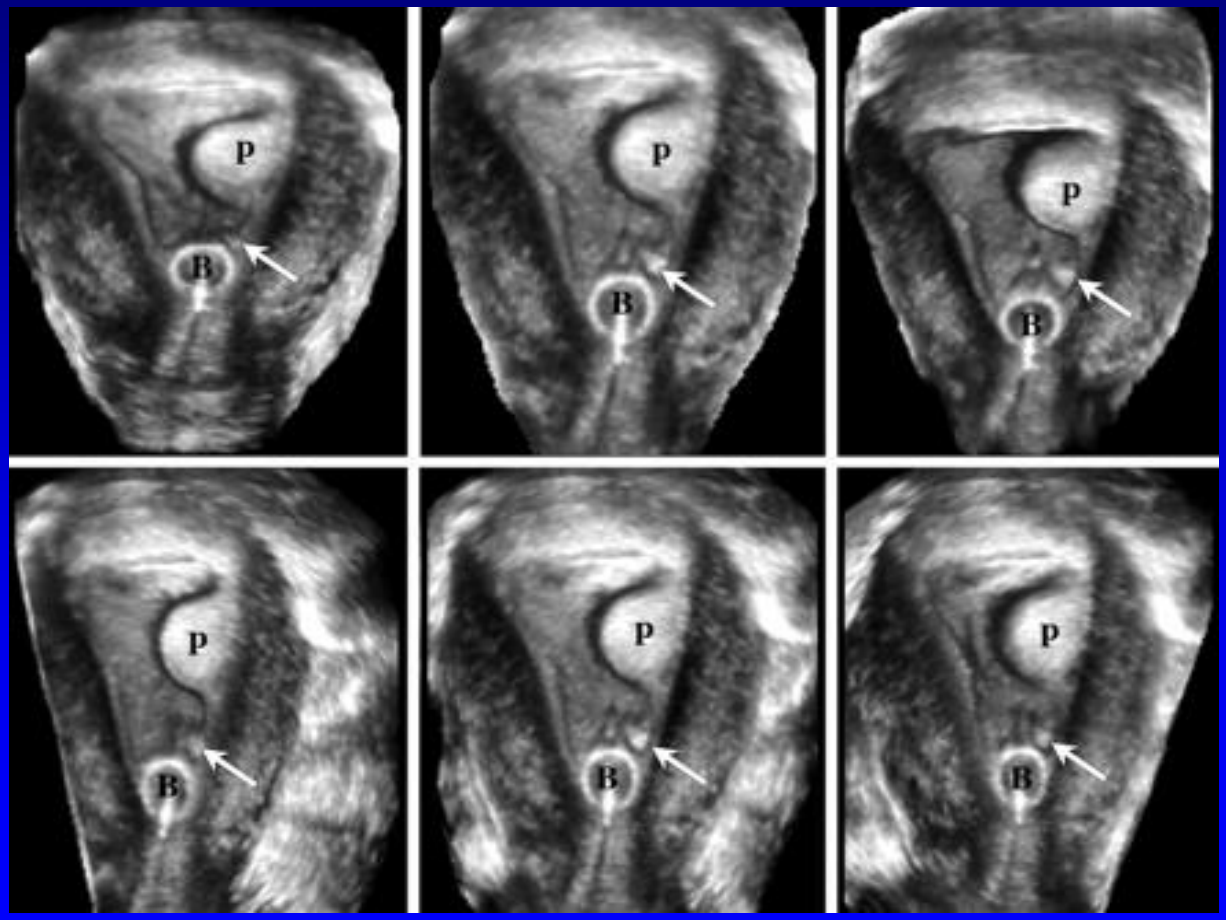
The commonest tumor in women:
20-25% in reproductive age women

Endometrial polyp





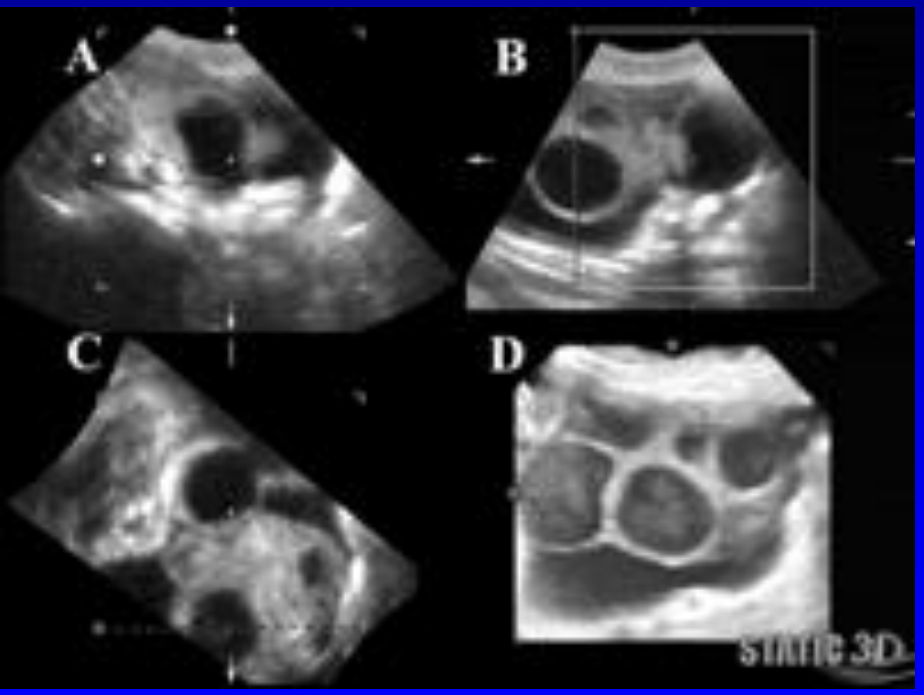
Endometrial polyp

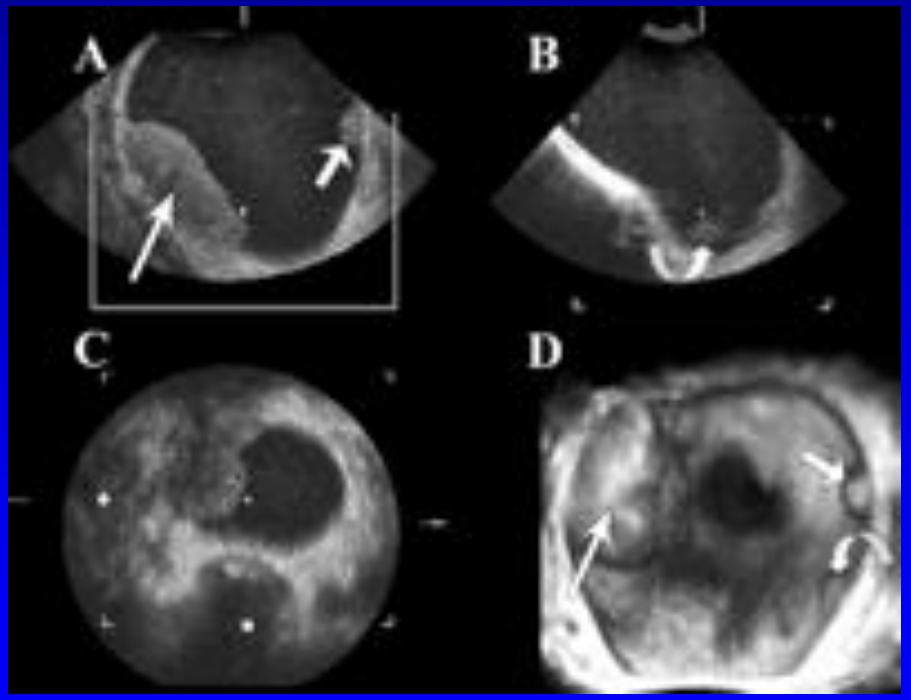


Ovary

1. Ovarian cyst
2. Polycystic ovary

Ovarian cyst





Polycystic ovary

Polycystic ovary: international consensus definitions

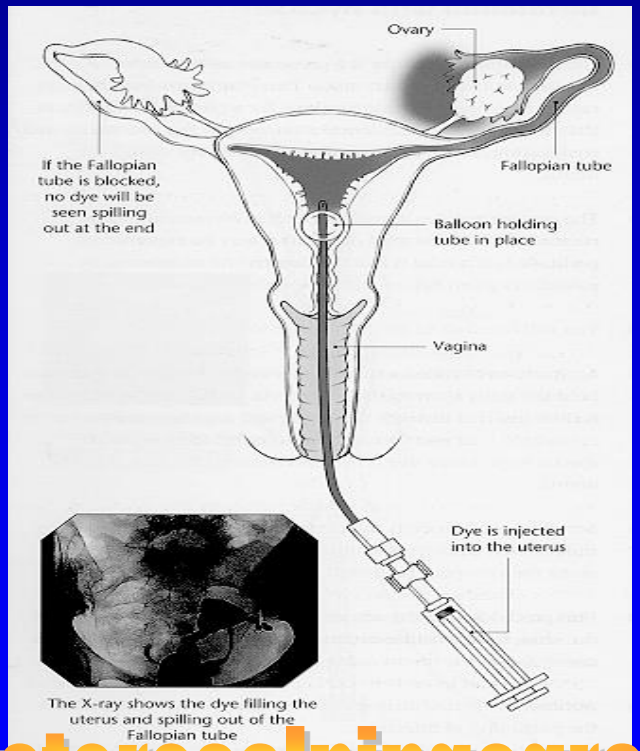
1. ≥12 follicles of 2-9 mm in diameter in at least one ovary or
2. Increased ovarian volume (>10 cm^3)

(Balen et al., 2003)

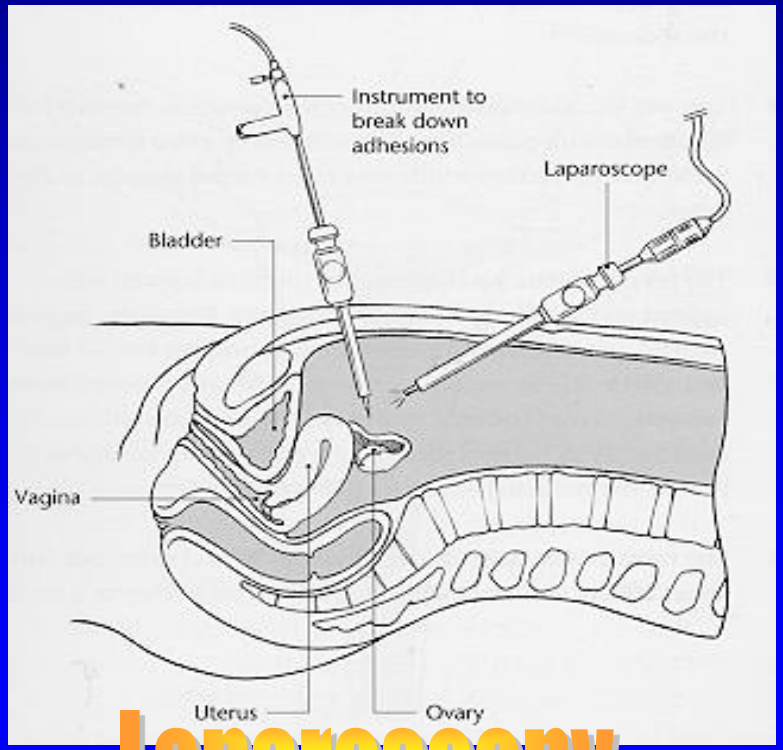
Fallopian tube

1. Tubal patency test
2. Hydrosalpinx

Tubal patency test



Hysterosalpingogram



Laparoscopy

3D Vs 2D sonohysterography

- Advantages over 2D sonohysterography
- Better visualization of a spill from the distal end of the tube (91% Vs 46%)
- Shorter duration of the procedure
- Lower volume of contrast medium

(Sladkevicius et al., 2000)

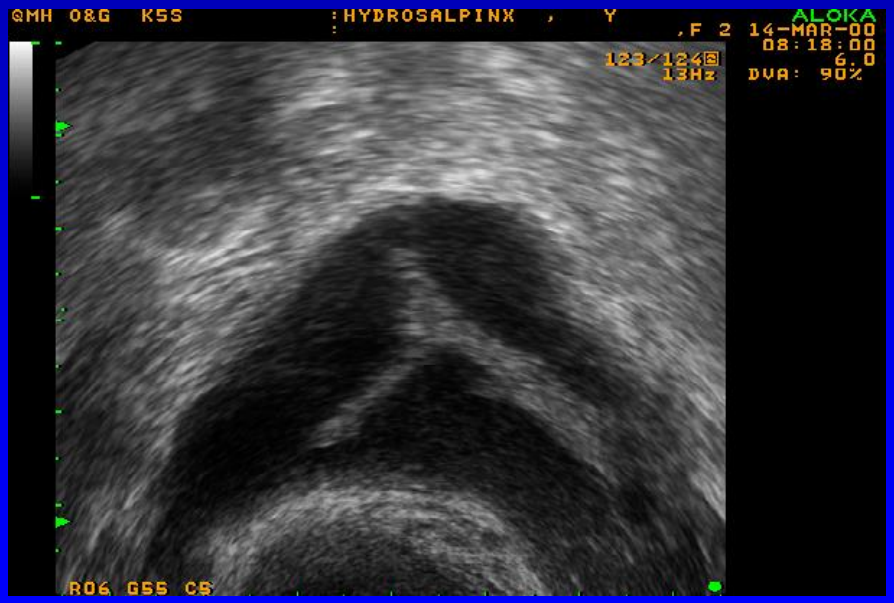
3D sonohysterography Vs laparoscopy

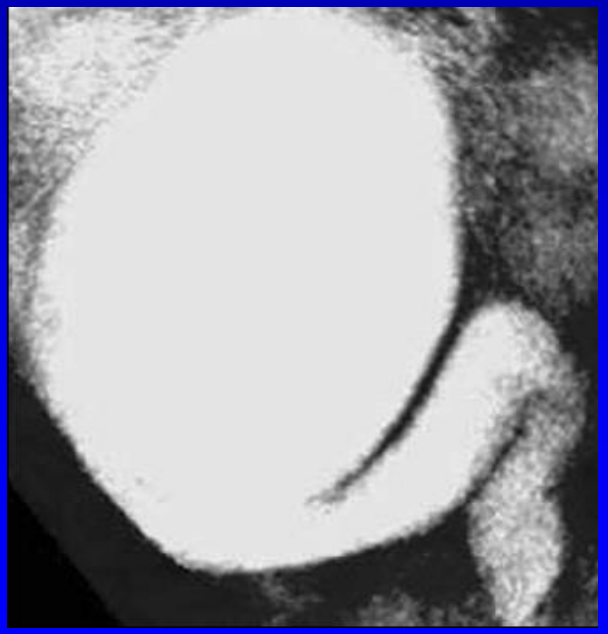
- The sensitivity of 3D sonohysterography for detecting tubal patency was 100% with a specificity of 67%.
- The positive and negative predictive values were 89% and 100% respectively
- The concordance rate was 91%.

(Chan et al., 2005)

Hydrosalpinx

- About 30% of infertile women seeking IVF treatment have hydrosalpinx





Ultrasound in reproduction

1. Subfertility workup
2. Assisted reproduction technique
   - Monitoring of ovarian response
   - Timing of the procedure
   - Oocyte retrieval / embryo transfer under ultrasound guidance
   - Prediction of ovarian response and pregnancy
- Early pregnancy scanning

Ultrasound in ART

Monitoring of ovarian response

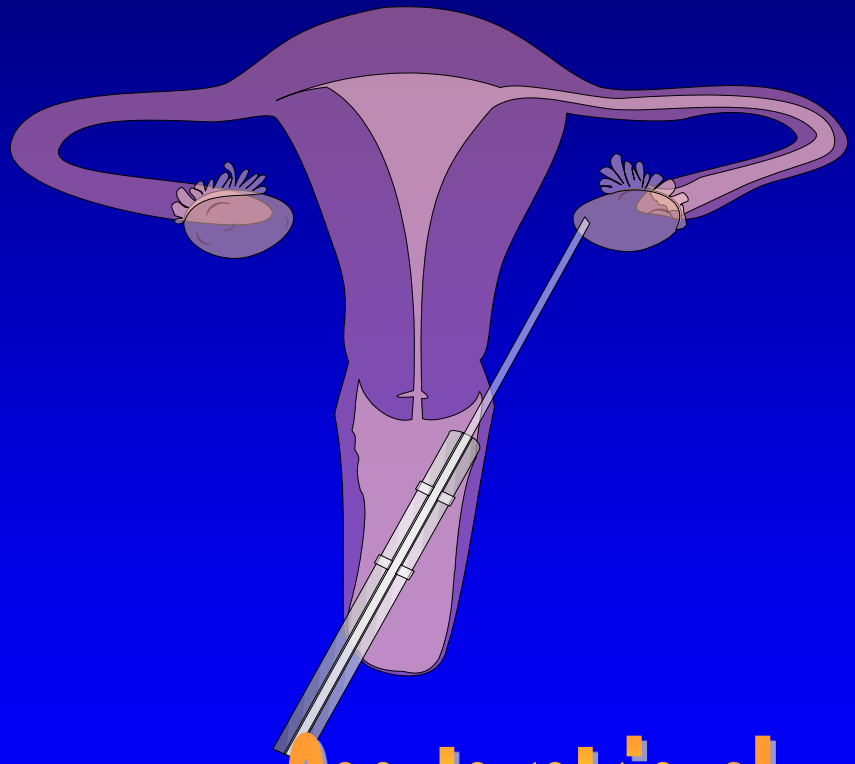
Ovulation induction

1. Clomiphene citrate
2. Gonadotrophin

Ovarian stimulation by gonadotrophin

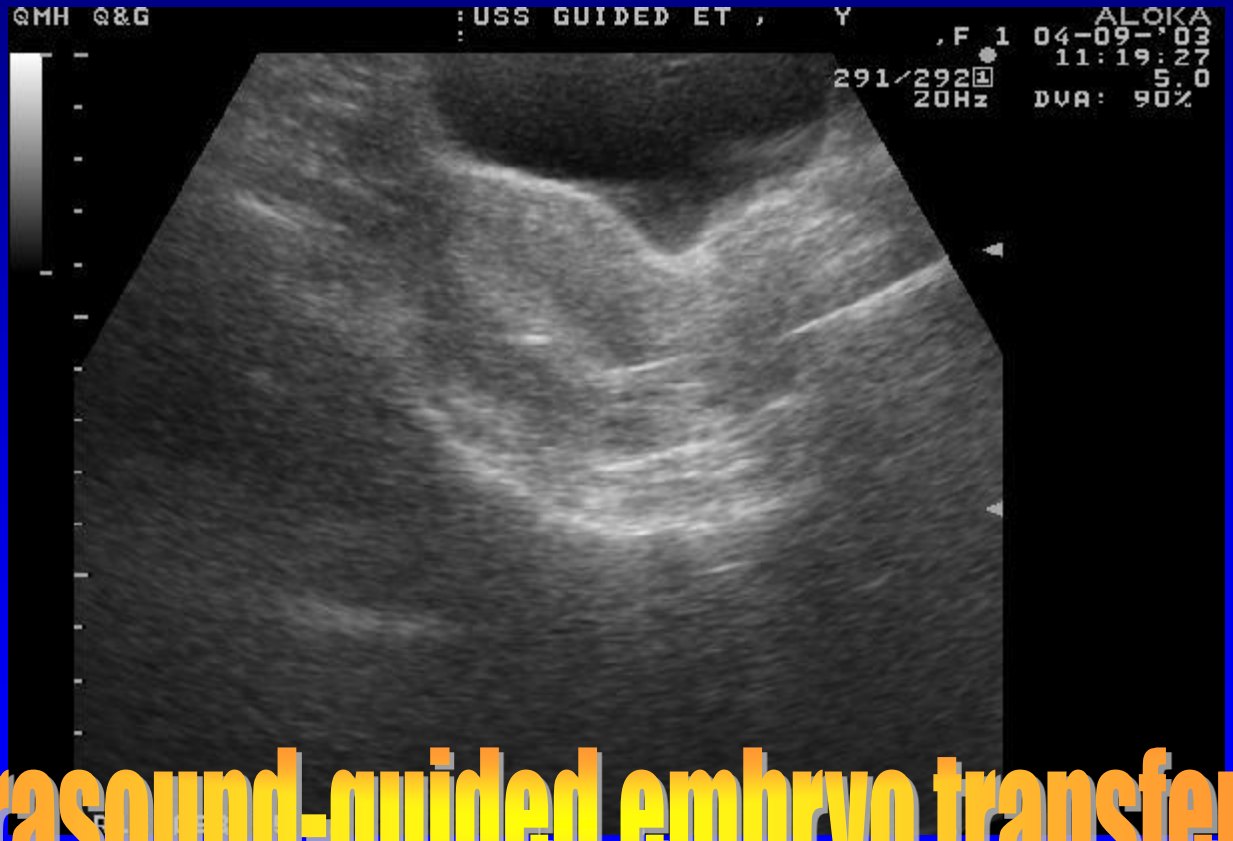
1. insemination
2. IVF

Ultrasound in ART



Oocyte retrieval

Ultrasound in ART

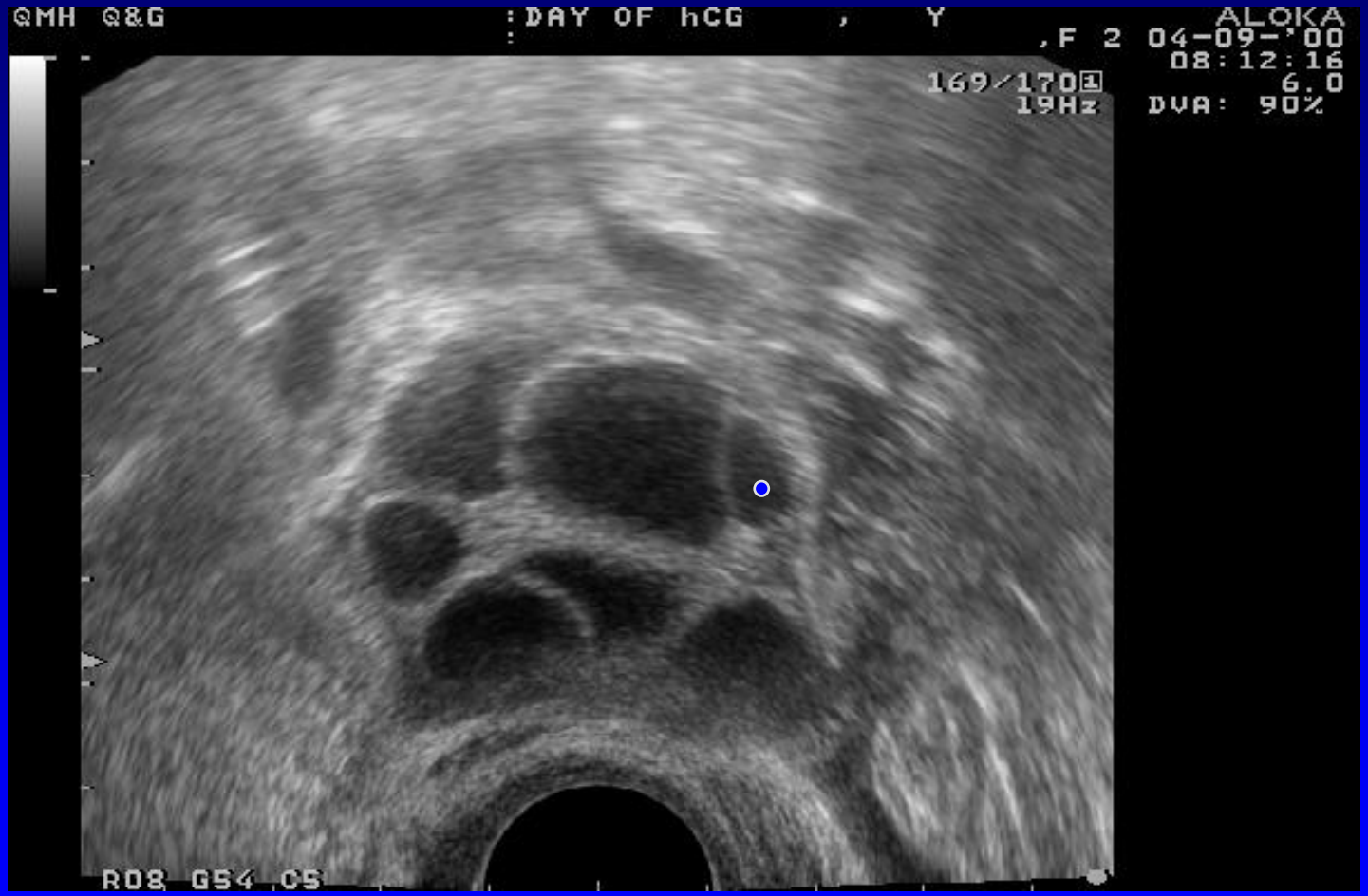


Ultrasound-guided embryo transfer

Ultrasound in reproduction

1. Subfertility workup
2. Assisted reproduction technique
   - Monitoring of ovarian response
   - Timing of the procedure
   - Oocyte retrieval / embryo transfer under ultrasound guidance
   - Prediction of ovarian response and pregnancy
- Early pregnancy scanning

Multiple follicular development



Concerns

- Poor ovarian responses
  - cycle cancellation
  - poor pregnancy rates
- Excessive ovarian responses
  - risk of ovarian hyperstimulation syndrome
  - high E2 detrimental to the outcome *(Ng et al., 2000)*

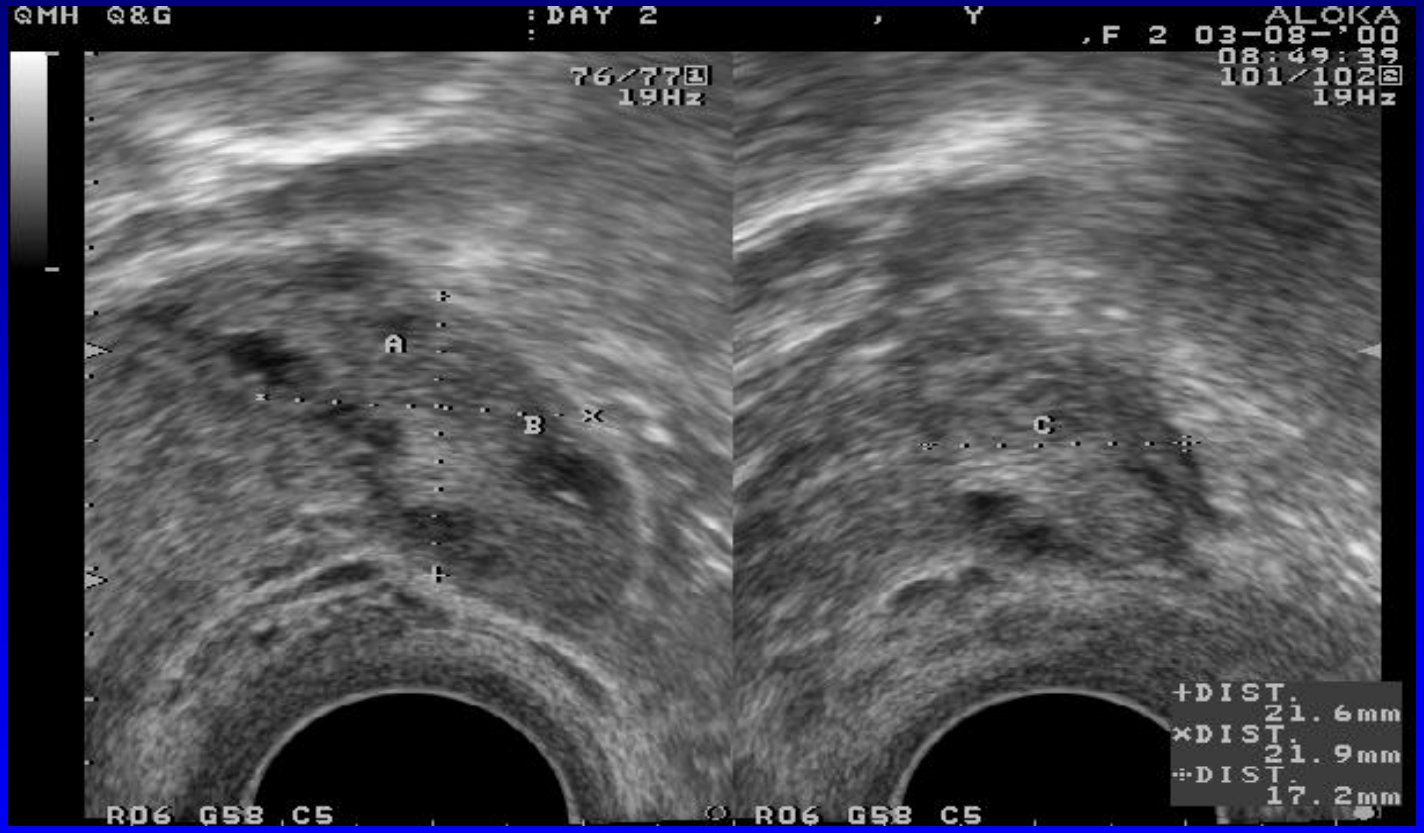
Ultrasound parameters

1. Ovarian volume *(Syrop et al., 1995; Lass et al., 1997)*

2. Antral follicle count *(Tomas et al., 1997; Chang et al., 1998a & 1998b; Ng et al., 2000; Fratarelli et al., 2000; Hsieh et al., 2001; Nahum et al., 2001; Kupesic and Kurjak, 2002; Popovic-Todorovic et al., 2003)*

3. Ovarian stromal blood flow *(Zaidi et al., 1996; Engmann et al., 1999; Kupesic and Kurjak, 2002; Kupesic et al., 2003; Popovic-Todorovic et al., 2003, Ng et al., 2005 & 2006)*

Ovarian volume



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Ovarian volume

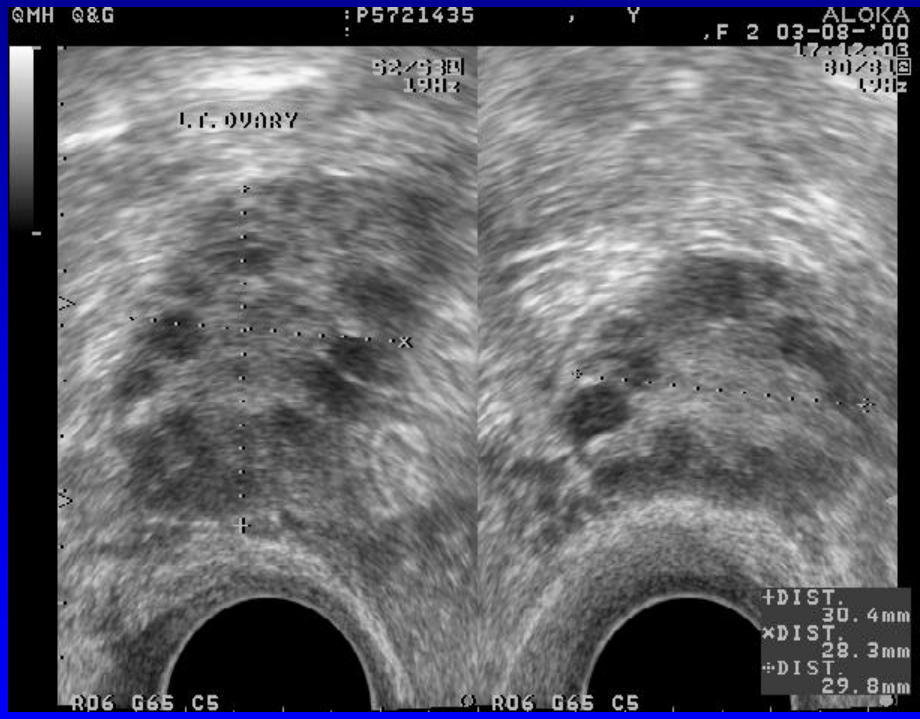
- Total ovarian volume and the volume of the smallest ovary predictive of peak E2 levels, no. of oocytes and cycle cancellation

(Syrop et al., 1995)

- Mean ovarian volume prior to stimulation predictive of poor ovarian response

(Lass et al., 1997)

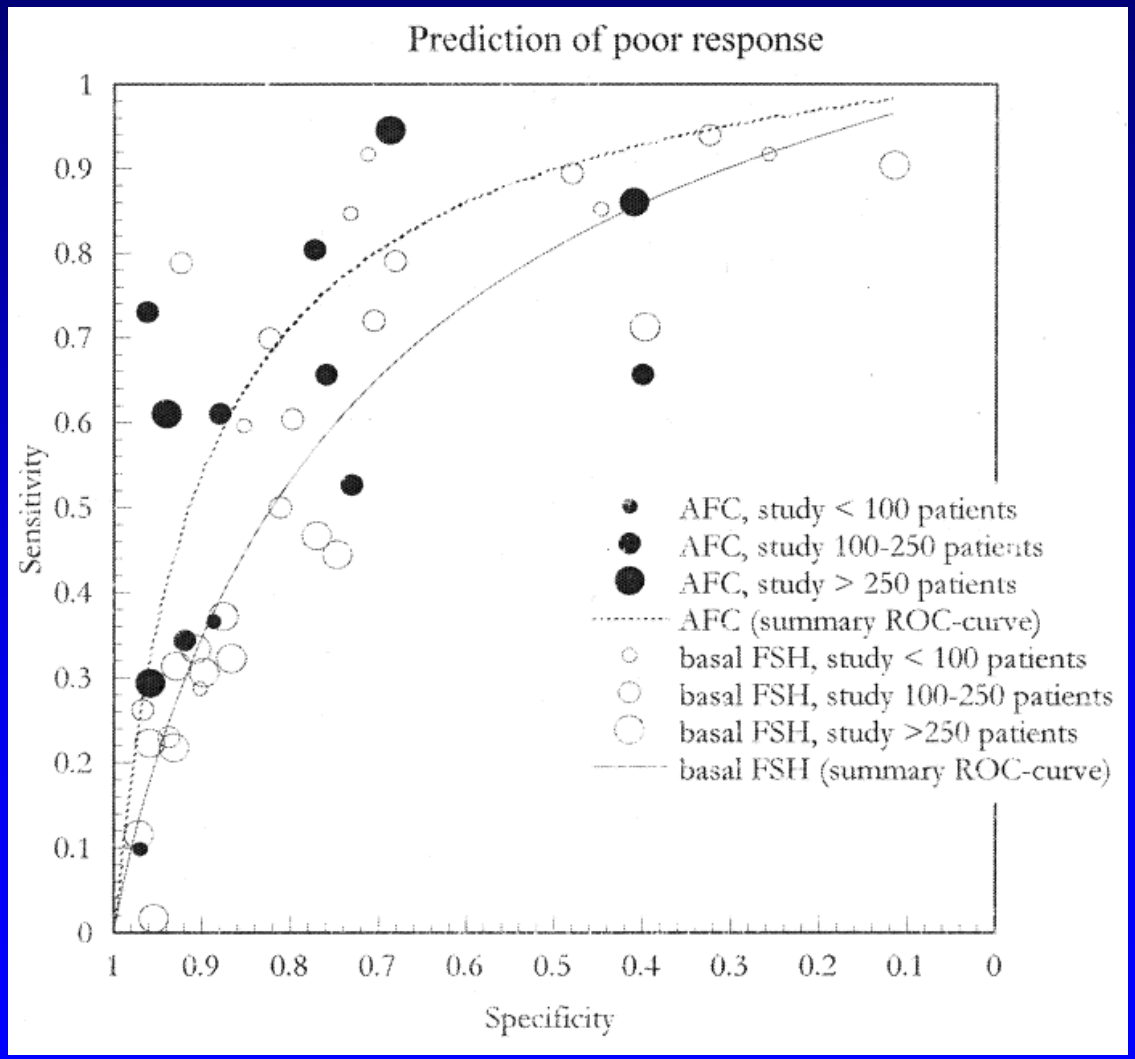
Antral follicle number (AFC)



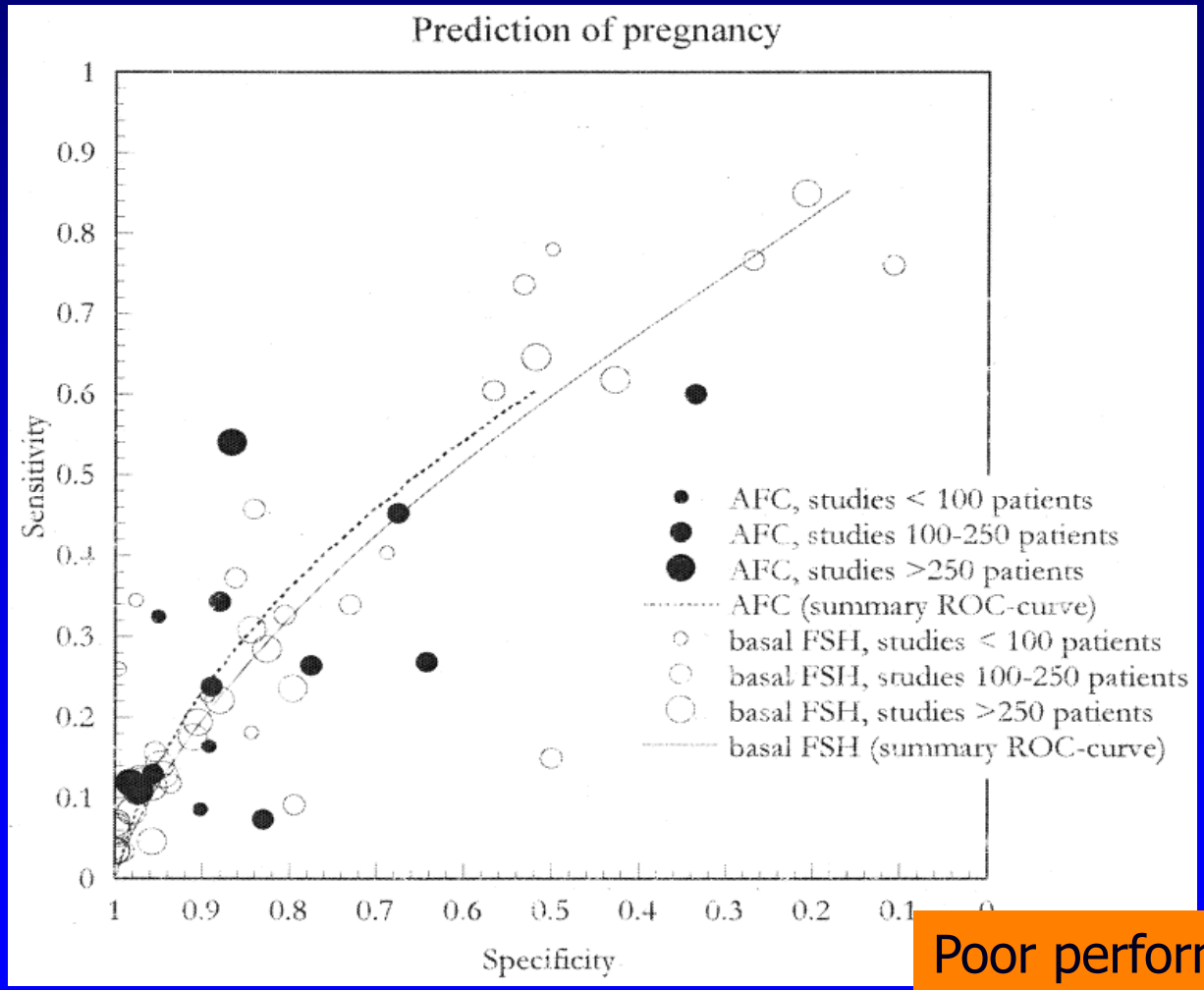
AFC

- AFC achieved the best predictive value of the number of oocytes obtained; followed by basal FSH, body mass index and age of women. *(Ng et al., 2000)*
- The predictive performance of AFC toward poor response is significantly better than that of basal FSH. AFC might be considered the test of first choice in the assessment of ovarian reserve prior to IVF. *(Hendriks et al., 2005)*

Summary ROC curves of AFC and FSH in prediction of poor response



Summary ROC curves of AFC and FSH in prediction of pregnancy



Poor performance for both AFC and FSH

Ovarian stromal blood flow

- Adequate vascular supply to provide endocrine and paracrine signals may play a key role in the regulation of follicle growth
- Normal responders had higher peak systolic velocity of ovarian stromal vessels than poor responders *(Zaidi et al., 1996; Engmann et al., 1999)*
- Women with RI >0.56 had longer stimulation duration and lower number of oocytes. *(Bassil et al.,1997)*

Ovarian stromal blood flow by 2D power Doppler

- No difference in ovarian responses between those with unilateral/bilateral absent ovarian stromal flow and bilateral ovarian stromal flow
- Ovarian stromal blood flow indices by 2D power Doppler had no predictive value for the ovarian response.

(Ng et al., 2005)

Ovarian stromal blood flow by 3D power Doppler

Number of oocytes obtained

	B (95% CI)	Beta	R^2 change	P value
AFC	0.421 (0.204, 0.638)	0.329	0.170	<0.001
Age	-0.516 (-0.809, -0.224)	-0.299	0.084	0.001
Body mass index	-0.388 (-0.720, -0.057)	-0.189	0.036	0.022

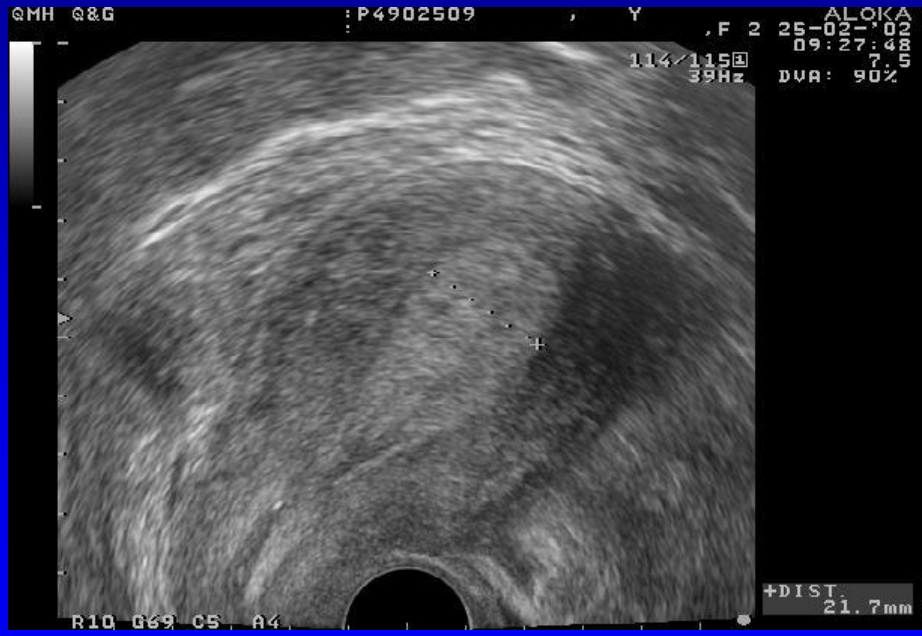
Basal FSH, mean ovarian volume, mean ovarian VI, FI and VFI were excluded in the equation.

(Ng et al., 2006)

Endometrial receptivity

1. Endometrial thickness and volume
2. Endometrial pattern
3. Doppler study of uterine vessels
4. Endometrial and subendometrial vessels
   - 2D Doppler flow indices
   - 3D Power Doppler indices: objective assessment of the blood flow towards endometrial and subendometrial regions

Endometrial thickness and pattern



Endometrial thickness and pattern

- Endometrial thickness: cut-off values between 6-10 mm to discriminate between pregnant and non-pregnant cycles
- Low positive predictive value and specificity in the prediction of the IVF outcome *(Turnbull et al., 1995; Friedler et al., 1996).*

Endometrial thickness

- Maximal value for endometrial thickness above which pregnancy is unlikely to occur ? >14mm
  - Reduced pregnancy rates noted by Weissman et al. (1999), Kupesic et al. (2001) and Schild et al. (2001)
  - Dickey et al. (1992) and Dietterich et al. (2002) demonstrated no adverse effects

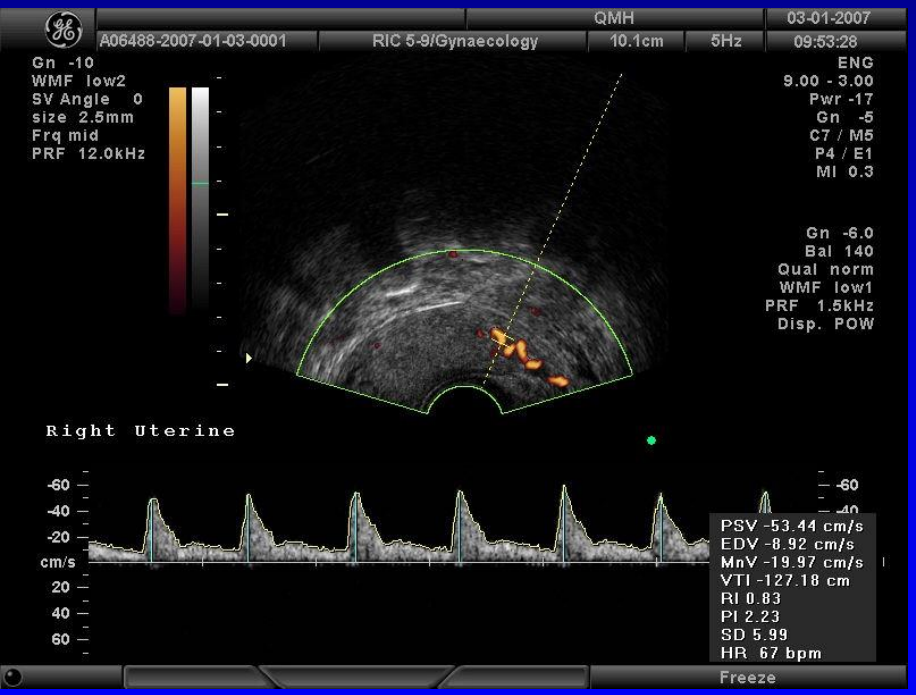
Endometrial volume

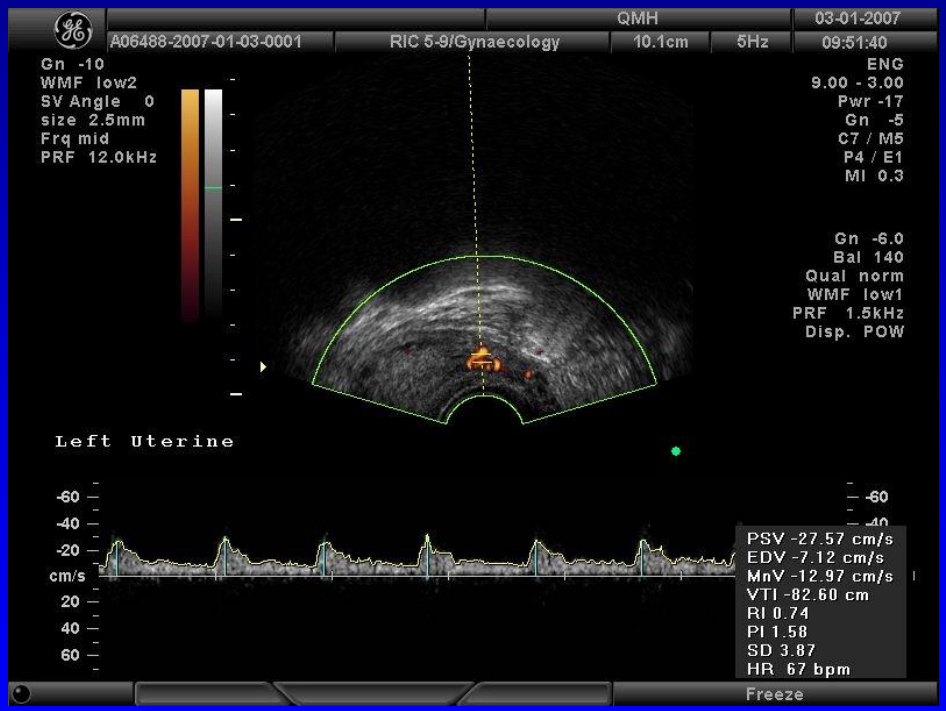
- Endometrium must attain at least 2.0-2.5 ml to achieve a pregnancy
- Endometrial volume measured on day of hCG *(Yaman et al., 2000),* egg collection *(Schild et al., 2001)* and embryo transfer *(Raga et al., 1999; Kupesic et al., 2001)* not predictive of pregnancy

Doppler study of uterine vessels

- Assessed by colour or power Doppler ultrasound and expressed as downstream impedance to flow
- Assumed to reflect the actual blood flow to the endometrium, although the major compartment of the uterus is the myometrium and there is collateral circulation between uterine and ovarian vessels.

Doppler study of uterine vessels





Doppler study of uterine vessels

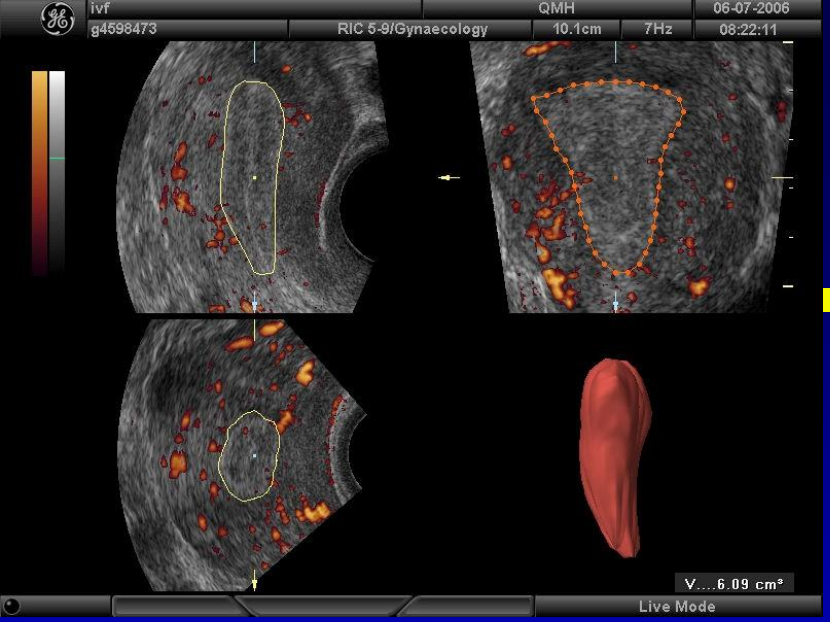
- Pregnancy decreased when uterine pulsatility index (PI) was ≥3.3-3.5, and the uterine resistance index (RI) was ≥0.95 *(Dickey, 1997).*
- Uterine PI has a high negative predictive value and sensitivity (in the ranges of 88-100% and 96-100%, respectively) and a relatively higher range of positive predictive value and specificity (44-56% and 13-35%, respectively). *(Friedler et al., 1996)*

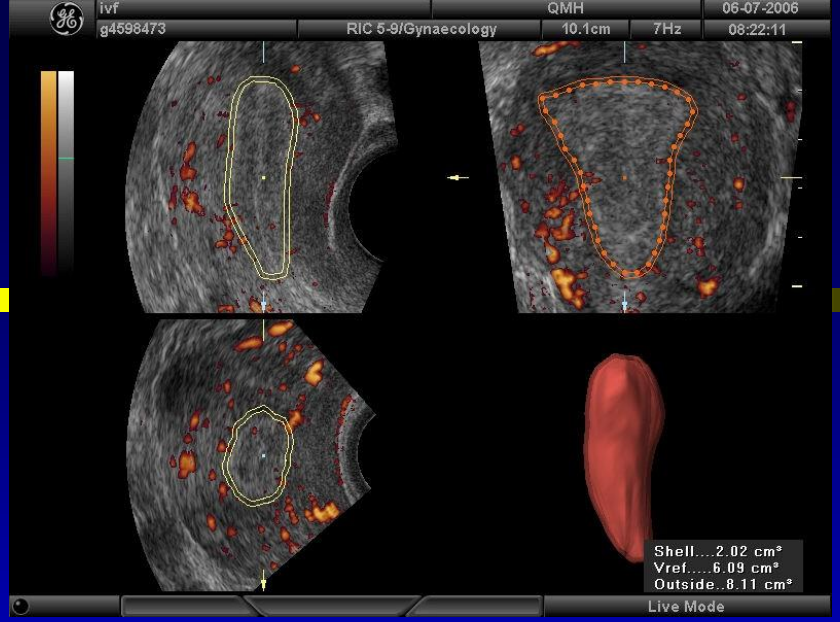
Doppler study of spiral arteries

- Not predictive of pregnancy *(Zaidi et al., 1995; Yuval et al., 1999; Schild et al., 2001)*, although *Battaglia et al. (1997)* and *Kupesic et al. (2001)* found significantly lower spiral artery PI in pregnant cycles than non-pregnant ones.

Endometrial blood flow

- A good blood supply towards the endometrium is essential for normal implantation.





Endometrial volume and blood flow

Subendometrial shell volume and blood flow

Table 3. Summary of studies of endometrial blood flow by 3D power Doppler ultrasound.

Study	IVF cycles	Inclusion/exclusion criteria	USS day	Results	Ref.
Schild *et al.* (2000)	75 cycles using a long protocol	Inclusion criteria Downregulation confirmed (endometrium <5 mm; no ovarian cyst of >2.5cm; serum estradiol <60 pg/ml)	Before stimulation	Subendometrial VI, FI and VFI lower in pregnant than nonpregnant cycles	[48]
	ET 2 days after OR	–	–	Subendometrial FI is the strongest predictive factor for IVF in logistic regression analysis	
Kupesic *et al.* (2001)	89 cycles using a long protocol Blastocyst transfer 5 days after OR	Inclusion criteria Serum FSH<10 Iu/l No fibroid, ovarian cysts and ovarian endometriosis	ET (hCG +7)	Higher subendometrial FI in pregnant cycles	[20]
Wu *et al.* (2003)	54 cycles (details of ovarian stimulation and ET not given)	Inclusion criteria: First cycle Age < 38 years Normal uterine cavity Serum FSH <15IU/L > = two good quality embryos	hCG	Higher subendometrial VFI in pregnant cycles	[49]
Dorn *et al.* (2004)	42 cycles using a long protocol	Exclusion criteria: Polycystic ovary syndrome Endometrium <6 mm Gynecological surgery	OR	No difference in subendometrial VI, FI and VFI between pregnant and nonpregnant cycles	[50]
Järvelä *et al.* (2005)	35 cycles using a long protocol ET 2 days after OR	Exclusion criteria: Uterine fibroids Endometriosis Single ovary Previous operation on uterus or salpingectomy	After stimulation and OR	No difference in endometrial and subendometrial VI between pregnant and nonpregnant cycles on both days	[26]
Ng *et al.* (2006b)	451 cycles using a long protocol ET 2 days after OR	Inclusion criteria: First cycle Normal uterine cavity	OR	Lower endometrial VI and VFI in pregnant cycles	[51]
Mercè *et al.* (2008)	80 cycles using a long protocol	Inclusion criteria: First cycle Normal uterine cavity Serum FSH <10 Iu/l Regular cycles Nonsmokers	hCG	Higher endometrial VI, FI and VFI in pregnant cycles	[29]