Forty-second Annual
Postgraduate Program

October 17, 2009
Atlanta, GA

Ultrasound In Reproductive Medicine Part I

Course 10

Sponsored by the
American Institute of
Ultrasound in Medicine
and the
American Society for
Reproductive Medicine

New Procedure to Obtain CME Credits

Dear Postgraduate Course Participant:

The Accreditation Council for Continuing Medical Education now requires that ASRM document learning for participants in CME programs. Thus, the procedure for claiming CME credits has changed. We ask your cooperation in following the steps below to ensure that your credits are provided correctly to you.

1. Within 3 days after the Annual Meeting you will be sent an email asking you to complete an online evaluation of this postgraduate course. A personalized Web link to the evaluation will be provided in your email. Please do not share this unique link.
2. In late November you will be sent a second email with a personalized Web link asking you to complete the post-test on the content of the course. This test is identical to the pre-test and will enable ASRM to assess the effectiveness of this postgraduate course as a learning activity. For your convenience, the test questions are printed in the course syllabus.

After both steps have been completed, you will be able to claim your CME credits and/or ACOG Cognates and receive a printable CME certificate. Please note that you must provide your 10-digit ACOG Membership Number to have your ACOG Cognates reported to ACOG. Results of both the course evaluation and the post-test are anonymous.

Both steps must be followed completely by **December 31, 2009** in order to receive CME credits. A maximum of 6.5 CME credits can be claimed for the postgraduate course. Please be aware that some email systems flag emails with Web links as junk mail, and you may need to check your junk-email folder for your notifications.

Please DO NOT forward the links. In case of difficulty please email *pfenton@asrm.org*

********Deadline for receiving CME credits = December 31, 2009********

Continuing Medical Education

Continuing medical education is a lifelong learning modality to enable physicians to remain current with medical advances. The goal of ASRM is to sponsor educational activities that provide learners with the tools needed to practice the best medicine and provide the best, most current care to patients.

As an accredited CME provider, ASRM adheres to the Essentials and policies of the Accreditation Council for Continuing Medical Education (ACCME). CME activities now must first, address specific, documented, clinically important gaps in physician competence or performance; second, be documented to be effective at increasing physician skill or performance; and third, conform to the ACCME Standards for Commercial Support.

AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE

Developed in Cooperation with the

AMERICAN INSTITUTE OF ULTRASOUND IN MEDICINE

ANNUAL MEETING POSTGRADUATE COURSE

ATLANTA, GA

OCTOBER 17, 2009

"ULTRASOUND IN REPRODUCTIVE MEDICINE PART I"

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All speakers at the 2009 ASRM Annual Meeting and Postgraduate Courses were required to complete a disclosure form. These disclosures were reviewed and potential conflicts of interest resolved by the Subcommittee on Standards of Commercial Support of the Continuing Medical Education Committee. The faculty has revealed the following information as potential conflicts of interest:

Alexander Hartman, M.D.: Nothing to disclose

Josef Blankstein, M.D.: Nothing to disclose

Olena Sagura, R.D.M.S.: Nothing to disclose

Bradley J. Van Voorhis, M.D.: Nothing to disclose

This activity may include discussion of off-label or otherwise non-FDA approved uses of drugs or devices.

Accreditation statement:
The American Society for Reproductive Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Designation statement:
The American Society for Reproductive Medicine designates this educational activity for a maximum of 6.5 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

American College of Obstetricians and Gynecologists (ACOG)
The American College of Obstetricians and Gynecologists has assigned 6.5 cognate credits to this activity.

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Please turn off/mute cell phones and pagers during the postgraduate course and all Annual Meeting sessions.

Thank you.

ULTRASOUND IN REPRODUCTIVE MEDICINE PART I

NEEDS ASSESSMENT AND COURSE DESCRIPTION

Can one imagine ART being performed today without imaging? Ultrasound has become an integral component not just of ART, but also of the daily practice of reproductive medicine, infertility, and gynecology. New practice guidelines for ultrasound in reproductive medicine have been published by AIUM in collaboration with ASRM in 2009 (J Ultrasound Med 28(1):125-138, 2009). Surveys of members of the Society for Reproductive Endocrinology and Infertility, the Imaging Special Interest Group, and ASRM have revealed a strong desire for continuing medical educaton in ultrasonography that would prepare reproductive medicine professionals and gynecologists for accreditation by the American Institute of Ultrasound in Medicine (AIUM). To accommodate physicians' educational needs, this course has been designed to be taken either as a two- or a one-day course. The curriculum for each day has been designed as a free standing course, so Part I is not a prerequisite for Part II.

The objectives of this course are to provide a comprehensive survey of the use of ultrasonography in the female pelvis for physicians, nurses and ultrasonographers actively involved in reproductive medicine, infertility and gynecology. There will be a live scanning demonstration during Part I to review the ultrasound techniques in performing a pelvic ultrasound examination. The faculty will review critically the application of ultrasonography to the evaluation, diagnosis, treatment and complications of infertility. Although ultrasonography has advanced early pregnancy evaluation and monitoring, the pitfalls and limits of diagnostic ultrasonography for assessment of pregnancy and its complications also will be addressed. Many other gynecologic findings on ultrasound such as congenital uterine anomalies, ovarian masses, tubal disease and other uterine pathologies will be discussed along with their impact on fertility. The course will cover a variety of reproductive problems throughout the reproductive lifespan from puberty through menopause from an ultrasound perspective. Newer technologies will also be discussed with current or potential application, such as 3D ultrasound and Doppler. Cases and controversies will offer the audience an opportunity to actively participate. Finally, the faculty will introduce the audience to the potential importance, requirements and benefits of AIUM accreditation.

ACGME COMPETENCY

Patient Care
Medical Knowledge

LEARNING OBJECTIVES

At the conclusion of this course, participants should be able to:

1. Summarize the appropriate use of ultrasonography in the evaluation of infertility, uterine abnormalities and the pathology of the reproductive tract.
2. Describe the proper assessment of early pregnancy and list findings on early pregnancy assessments that are associated with poor outcomes.
3. Discuss new developments in ultrasonography, the importance of 3-D ultrasonography in reproductive medicine, and the importance of Doppler blood flow assessment in reproductive medicine and gynecology.
4. List the requirements and benefits of a clinical practice attaining accreditation in ultrasonography.

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OCTOBER 17, 2009

"ULTRASOUND IN REPRODUCTIVE MEDICINE PART I"

Alexander Hartman, M.D., Chair

Saturday, October 17, 2009

08:15 – 08:30	Course Introduction and Orientation **Alexander Hartman, M.D.**
08:30 – 09:05	Ultrasound Assessment in the Infertility Evaluation **Bradley J. Van Voorhis, M.D.**
09:05 – 09:15	Questions and Answers
09:15 – 09:50	Ovulation Induction and Ovarian Hyperstimulation Syndrome **Josef Blankstein, M.D.**
09:50 – 10:00	Questions and Answers
10:00 – 10:30	Break
10:30 – 11:05	Ultrasound Diagnosis of Uterine Anomalies and It's Effect on Fertility **Alexander Hartman, M.D.**
11:05 – 11:15	Questions and Answers
11:15 – 11:50	Ultrasound Assessment of the Ovary **Bradley J. Van Voorhis, M.D.**
11:50 – 12:00	Questions and Answers
12:00 – 13:00	Lunch
13:00 – 13:45	Live Scanning: Tricks to Improve Your Ultrasound Assessment **Alexander Hartman, M.D., Olena Sagura, R.D.M.S.**
13:45 – 14:00	Questions and Answers
14:00 – 14:45	Ultrasound Findings in PCOS – Current Controversy **Bradley J. Van Voorhis, M.D.**

Saturday, October 17, 2009 (continued)

14:45 – 15:00	Questions and Answers
15:00 – 15:30	Break
15:30 – 16:05	Early Pregnancy Failures Following IVF **Josef Blankstein, M.D.**
16:05 – 16:15	Questions and Answers
16:15 – 16:50	Controversial Issues, Cases, and a Few Remarks on AIUM Accreditation **All Faculty**
16:50 – 17:00	Questions and Answers

ULTRASOUND ASSESSMENT IN THE INFERTILITY EVALUATION

Brad Van Voorhis, M.D.
Department of Obstetrics and Gynecology
University of Iowa College of Medicine
Iowa City, Iowa

LEARNING OBJECTIVES

At the conclusion of this presentation, participants should be able to:

1. Explain the role of ultrasonography in the infertility evaluation.
2. List the adverse effects of fibroids on reproduction.
3. Discuss the impact of polyps and hydrosalpinges on fertility.

Ultrasound Assessment in the Infertility Evaluation

Brad Van Voorhis, M.D.
Department of Obstetrics and Gynecology
University of Iowa College of Medicine
Iowa City, Iowa

Learning Objectives

At the conclusion of this presentation, participants should be able to:

1. Explain the role of ultrasonography in the infertility evaluation.
2. List the adverse effects of fibroids on reproduction.
3. Discuss the impact of polyps and hydrosalpinges on fertility.

Disclosure:

Brad Van Voorhis, M.D.

I was a co-investigator on a study for ViaCell (study has since ended).

Traditional Evaluation for Infertile Couple

- History and physical exam
- Tubal patency
  - Chlamydia antibodies
  - Hysterosalpingogram (HSG)
  - Laparoscopy
- Semen analysis
- Assessment of ovulation
  - Basal body temperature (BBT)
  - Progesterone level
  - Luteinizing hormone (LH) detection

What is role of ultrasound?

Ultrasound in Infertility Assessment

Uterus
- Fibroids
- Polyps
- Endometrial receptivity/fluid

Ovary
- Ovarian cysts
- Ovarian reserve
- Polycystic ovaries

Fallopian tube
- Hydrosalpinges
- Tubal patency

Ultrasound in the Infertile Patient

- Transvaginal ultrasound is accurate in detecting pelvic pathology except for:
  - Pelvic adhesive disease (especially filmy adhesions)
  - Mild endometriosis
- Allows for delay or elimination of laparoscopy

Ubaldi et al. Hum Reprod 1998;13:330-3

Prevalence of Abnormal Findings in Infertile Women

	Infertile	Abnormal uterine bleeding	Abnormal bleeding	Fertile controls
N	600	409	80	100
Polyps	13%	30%	32.5%	10%
Intramural fibroids	20%	37%	57%	13%
Submucous fibroids	3%	9%	21%	1%
Arcuate uterus	15%	6%		

Are abnormalities more common in infertile women than fertile controls?

Tur-kaspa et al. Fertil Steril 2006;86:1731-5

Clevenger-Hoeft et al. Obstet Gynecol 1999;94:516-20

Are Fibroids Associated with Infertility?

We do not know:

- No large scale studies showing increased prevalence in infertile versus fertile women
- Many women with infertility have fibroids.
- Many women with fibroids easily conceive.
- "Clinical opinion" states fibroids play a role in 2%-3% of infertility patients.

Fibroids and IVF Outcome: Iowa Experience

Matched follow-up study

- Matched for age, number of embryos transferred, embryo grade
- N=91 women with fibroids, 91 controls
- Screening
  - Transvaginal ultrasound
  - HSG within 12 months
- Excluded: intracavitary lesion
- Fibroids
  - Average size: 2.8 cm (1-5 cm)
  - Average number: 1.8±.8
  - 98% fundal, 95% intramural

Stovall et al. Hum Reprod 1998;13:192-7

Fibroids and IVF Outcome: Iowa Experience

	Fibroids	Controls
Clinical pregnancy rate	37%*	53%
Delivery rate	33%*	48%
Implantation rate	14%*	20%
No difference in miscarriage rate		

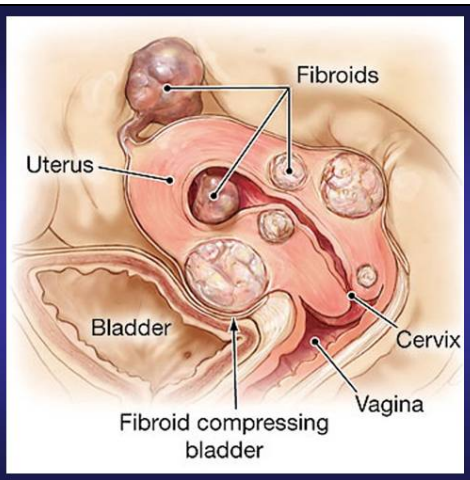
* P< 0.05

Stovall et al. Hum Reprod 1998;13:192-7

Pregnancy Rates After IVF with Uterine Fibroids

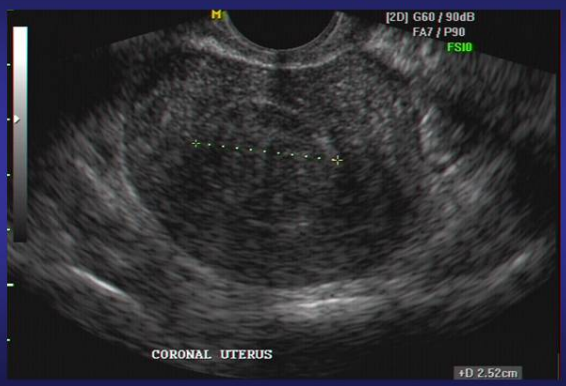
Study	Fibroids: No cavity distortion	Fibroids: Distorts cavity	Control
Surrey	49%		57%
Stovall	33%*		48%
Eldar-Geva	34%	10%-16%*	30%
Farhi	25%	9%*	29%
Hart	15%*		28%
Check	20%		38%
Khalaf	15%*		24%

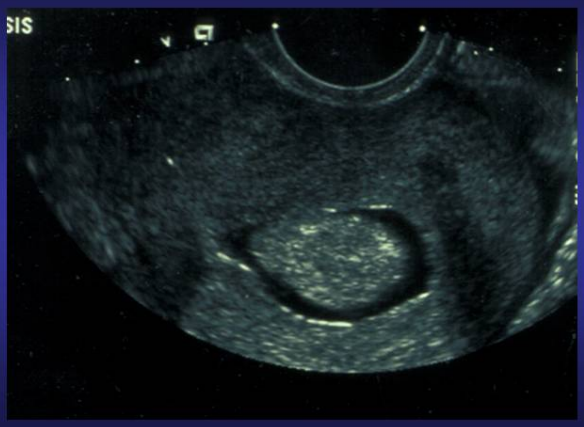
Surrey et al. Curr Opin Obstet Gynecol 2003;15:239-42
Khalaf et al. Hum Reprod 2006;21:2640-4



Van Voorhis. JAMA 2009;301:82-93

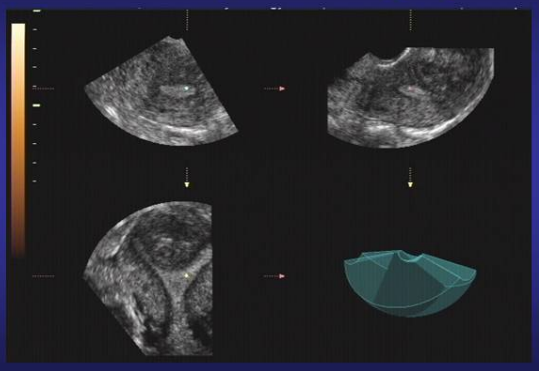
Intracavitary Myoma





Fibroid Near Cavity

Fibroid by 3-D Imaging



Conclusions from IVF Studies

Fibroids affecting cavity impair pregnancy rates.
Methods to detect cavity distortion are important (saline infusion sonography [SIS]/hysteroscopy better than HSG).
3-D ultrasound may help.

Intramural myomas may have a more subtle impact (many studies excluded large myomas).
No evidence that myomectomy for intramural fibroids improves IVF success.

Spontaneous Loss Rate in Women with Fibroids

- Ultrasound-based prospective study
- All singleton gestations in first trimester
- Fetal cardiac activity (FCA) seen
- Nearly all fibroids were intramural

	No fibroids	Fibroids
N	715	143
Assisted conception	6.4%*	14.7%
Mean age	32.9	33.1

*$p < 0.05$

Benson et al. J Clin US 2001;29:261-4

Pregnancy Outcome Based on Number of Fibroids

Number of fibroids	Number of patients	Liveborn rate	Spontaneous pregnancy loss rate
No fibroids, normal uterus	715	92.4%	7.6%
Single fibroid	88	92.0%	8.0%
Multiple fibroids	55	76.4%	23.6%*
Two	25	76.0%	24.0%
Three	8	87.5%	12.5%
Four or more	22	72.7%	27.3%

*$p < 0.05$ (Fisher's exact test) for comparison of loss rate with single versus multiple fibroids. Size of fibroids did not make a difference.

Benson et al. J Clin US 2001;29:261-4

Fibroids and Pregnancy Outcomes – Ultrasound Diagnosis

	Fibroids	Controls
N	492	12,216
Age	31.6	31.3
Threatened Ab	17.1%*	10%
Abortion	7.7%	6.8%
Premature delivery	9.3%	9.0%
Abruption	7.5%*	.9%
Pelvic pain	12.6%*	.1%

*$p < 0.05$

No difference in fetal growth, cesarean section rates

Abruption and pain related to size of fibroid

Abruption related to placenta located over fibroid

Exacoustós and Rosati. Obstet Gynecol 1993;82:97-101

Fibroids and Pregnancy Outcomes

- Others have confirmed an increased risk of abruption and pelvic pain (10-15%).
- Some have noted an increase in preterm labor and cesarean section rates.

Davis et al. Obstet Gynecol 1990;74:41-4
Katz et al. Obstet Gynecol 2004;16:239-43

Adenomyosis

Histology – heterotopic endometrial glands and stroma with adjacent smooth muscle hypertrophy

Ultrasound findings

- Enlarged uterus (no fibroids)
- Poor definition of endomyometrial junction
- Myometrial cysts
- Variable echogenicity (hypoechoic areas common)
- Absence of mass effect
- Poor lesion borders
- Penetrating blood supply (peripheral in fibroids)

Adenomyosis

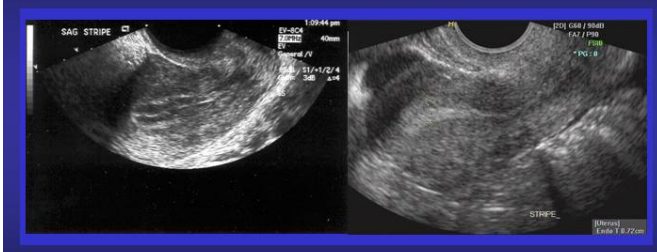
Adenomyosis – Diagnostic Accuracy

	Ultrasound	MRI
Sensitivity	53-70%	70-82%
Specificity	65-90%	85-90%
⊕ predictive value	50-90%	60-90%
⊖ predictive value	85-95%	86-95%

Lone et al. J Obstet Gynecol 2006;26:225-8

MRI = magnetic resonance imaging

Changes in Endometrium During the Menstrual Cycle



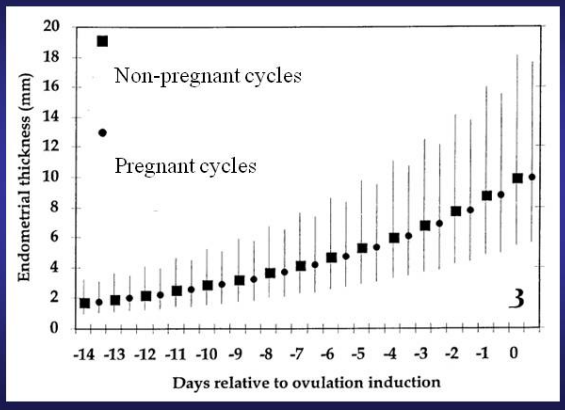
Proliferative (left) and secretory (right) endometrium

Ultrasound Appearance of the Endometrium in 1186 Infertile Women

- Growth of endometrium follows an exponential curve in both natural and stimulated cycles.
- Maximal thickness correlates with estradiol levels, but not a woman's age.
- Mean maximal thickness is lower in natural cycles.

	Mean endometrial thickness (mm)	Range (mm)
Natural	9.9	5.2-18.0
Stimulated (long protocol)	11.5	6.5-19.0

De Geyter et al. Fertil Steril 2000;73:106-13



De Geyter et al. Fertil Steril 2000;73:106-13

Observations on Endometrial Stripe Thickness in Donor Egg Cycles

Clinical pregnancy rates relative to recipient mid-cycle mean endometrial thickness

Endometrial thickness	Clinical pregnancy rate n (%)	Live-birth rate n (%)[a]
<6 mm	2/10 (20%)[b]	2/10 (20%)[d]
6 mm	16/32 (50%)	14/32 (44%)
7 mm	34/64 (53%)	27/64 (42%)
8 mm	29/59 (49%)[b]	23/59 (40%)[d]
≥9 mm	110/162 (68%)[c]	93/162 (57%)[e]

[a] Numbers represent number of pregnant cycles/number of cycles
[b vs c] $P < .02$
[d vs e] $P .05$ (determined by the χ^2 test)

Noyes et al. Fertil Steril 2001;76:92-7

Blood Flow and Endometrial Receptivity

- Some report decreased implantation rates if uterine artery pulsatility index (PI) is ≥ 3.3 or absence of early or end diastolic flow – others do not.
- Endometrial and subendometrial blood flow by power Doppler:
  - Increases in follicular phase (peak – 3 days before ovulation, declines 5 days post-ovulation).
  - Is lower in older women.
  - Does not appear to be good predictor of implantation.

Järvelä et al. US Obstet Gynecol 2005;26:765-9
Ng et al. Hum Reprod 2006;21:1612-7

Bottom Line

- Blood flow in the endometrium in the assessment of infertility:
  - Remains experimental at this time.

Who Needs SIS? When Is the Endometrium Too Thick?

- Some propose a 5-mm cut-off in bleeding patients.
- Not evaluated in infertile patients.
- Advice is to use liberally; we use if:
  - 1. Endometrium is irregular.
  - 2. Endometrium not well seen.
  - 3. Endometrium greater than 10 mm in thickness

Breitkopf et al. Obstet Gynecol 2004;104:120-5

Accuracy of Diagnostic Tests for Polyps

N = 65 infertile women age 19-43 years

Gold standard = hysteroscopy

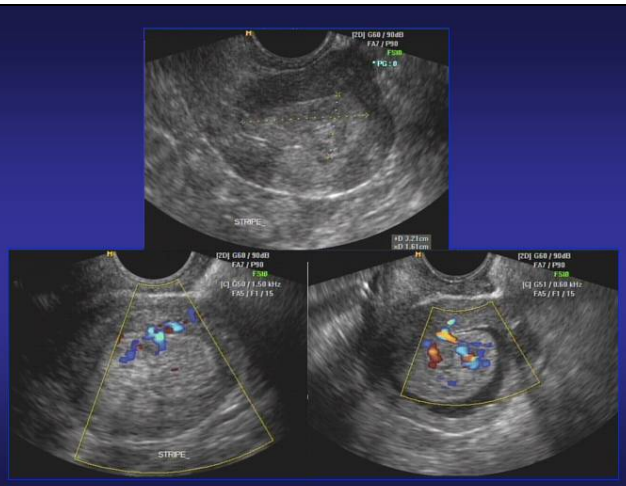
	Sens (%)	Spec (%)	PPV (%)	NPV (%)
HSG	50	82	29	92
TVS	75	96	75	96
SIS	100	100	100	100

SIS also better for uterine malformations

SIS + HSG similar for uterine adhesions (high false ⊕ rate)

Sens = sensitivity
Spec = specificity
PPV = positive predictive value
NPV = negative predictive value
TVS = transvaginal sonography

Soares et al. Fertil Steril 2000;73:406-11

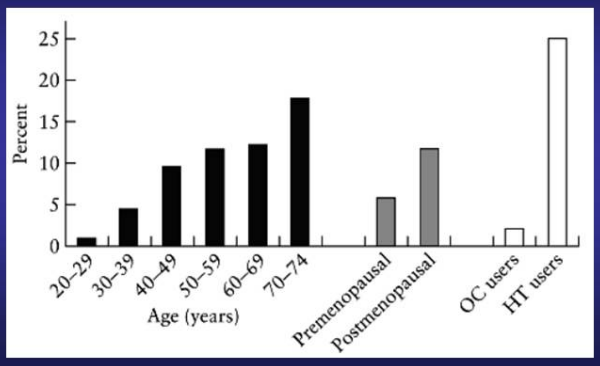


Prevalence of Endometrial Polyps

- 618 of 1660 women in Denmark participated (randomly selected from Danish Civil Registration System).
- Age 20 – 74 (median 45) years of age
- All completed a questionnaire regarding menstrual bleeding.
- All had ultrasound and SIS.

Dreisler et al. US Obstet Gynecol 2009;33:102-8

Prevalence of Uterine Polyps



Dreisler et al. US Obstet Gynecol 2009;33:102-8

Findings of Study

- Overall prevalence of polyps – 7.8%
- Polyps rare (0.9%) below age 30 years
- Polyp prevalence increases with age.
- Polyps rare in women on oral contraceptive pilss (OCPs); more common in women on hormone therapy (HT)
- Obesity is a risk factor (OR 2.06; 1.12 – 3.79)
- Malignancy uncommon (1.5%) in polyps
- Polyps not associated with menstrual bleeding complaints - in this study

OR = odds ratio

Dreisler et al. US Obstet Gynecol 2009;33:102-8

Prevalence of Endometrial Polyps

- May vary by technique used to diagnose and patient age.
- Beware of artifacts (fragments from dilation-hysteroscopy, clots, thickened secretory endometrium).
- Prevalence is 5%-10% among infertile couples for IVF and higher (18%) in couples who have failed multiple IVF cycles.

Oliveria et al. Fertil Steril 2003;80:1371-5
Seinera et al. Acta Obstet Gynecol Scand 1988;76:135-7

Polyps and Infertility

- Uncertain if prevalence higher in infertile women
- Crude pregnancy rates after removal 23% – 65%/year
- Location (utero-tubal junction) and size (variable in different studies) may influence polyp's effect on fertility

Yanaihara et al. Fertil Steril 2008;90:180-2

Effect of Polyps on Fertility

Limited data:
Polyps <2 cm may have no effect on IVF pregnancy rate, but increase miscarriage rates (Bourne Hall).

	Polypectomy	Hysteroscopy + Biopsy
N	101	103
Pregnancy rate (4 hMG-IUI cycles)	63%*	28%

No relationship to size of polyp *P <0.001

hMG = human menopausal gonadotropin
IUI = intrauterine insemination

Lass et al. J Assist Reprod Genetics 1999;16:410-5
Perez-Medina et al. Hum Reprod 2005;20:1632-5

Ultrasound Findings with Hydrosalpinges

- Sonolucent or low-level echoes
- Wall thickness – varies
- Incomplete septa
- "Beads on a string" or "cogwheel sign"
- Serpiginous shape

Hydrosalpinx

Hydrosalpinges and IVF

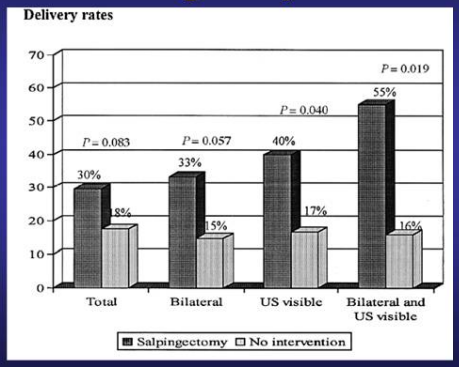
- Retrospective analyses have demonstrated that the presence of a hydrosalpinx impairs the outcome from IVF:
  - Pregnancy rates reduced by 50%
  - Miscarriage rates are increased 2-fold.
  - Possible increase in ectopic pregnancy rates

Theories About the Negative Effect of Hydrosalpinges on IVF

- Embryo-toxic properties of fluid
- Endometrial alterations by fluid
- Mechanical "wash-out" of embryos

Hydrosalpinx fluid is sterile, but may have increased levels of endotoxin

Effect of Salpingectomy on IVF Pregnancy Rates



Strandell et al. Hum Reprod Update 2000;6:387-95

Transvaginal Aspiration of Hydrosalpinges at Oocyte Retrieval

	Treatment group		
	Aspiration n (%)	No aspiration *n* (%)	*P*
Sowter *et al.* 1997			
Clinical pregnancy rate	6/30 (20.0)	3/18 (16.7)	n.s.
Delivery rate	5/30 (16.7)	3/18 (16.7)	n.s.
Implantation rate	7/85 (8.2)	4/53 (7.5)	n.s.
Mean no. of embryos transferred	2.84	2.86	
Van Voorhis *et al.* 1998			
Clinical pregnancy rate	5/16 (31.3)	1/18 (5.6)	n.s.
Delivery rate	5/16 (31.3)	0	0.015
Implantation rate	8/58 (13.8)	1/71 (1.4)	0.011
Mean no. of embryos transferred	3.6	3.8	

Causes of Fluid in Endometrial Cavity

- Hydrosalpinges
- Polycystic ovary syndrome (PCOS) (rarely)
- ? Uterine infection – subclinical
- ? Cesarean section scar
- Physiologic

Sharara and McClamrock. Hum Reprod 1997;12:2816-19
Sharara and Prough. J Reprod Med 1999;44:299-302

Endometrial Fluid and IVF

Tubal disease and fluid
- Lower pregnancy rates

PCOS and fluid
- No effect

Akman et al. Hum Reprod 2005;20:906-9

Endometrial Fluid in IVF Cycles

- Develops in 8% of cycles
- Fluid before hCG administration
  - Higher cancellation rate for poor response
    - 30% vs. 17%
  - Lower pregnancy rate
    - 26% vs. 42% (mainly due to cancellations)
- Fluid after hCG administration
  - No effect (some were aspirated)

Abstracts of 17th Annual Meeting of ESHRE. Hum Reprod 2001;16:210-15

hCG = human chorionic gonadotropin

Effect of Endometrial Fluid at Time of Oocyte Retrieval on IVF Pregnancy Rates

All tubal embryo transfer cycles

	Fluid accumulation >1 mm	No fluid
n	10 (5%)	185
Pregnant	7 (70%)	98 (53%)
IR	29%	26%

No difference if fluid is "physiologic"

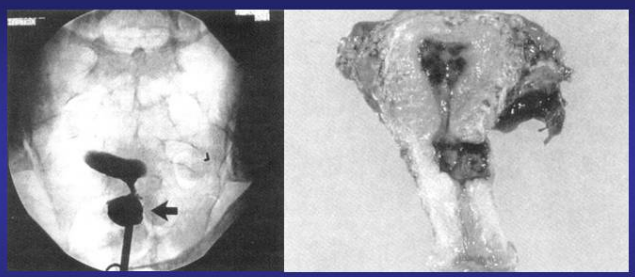
IR = implantation rate

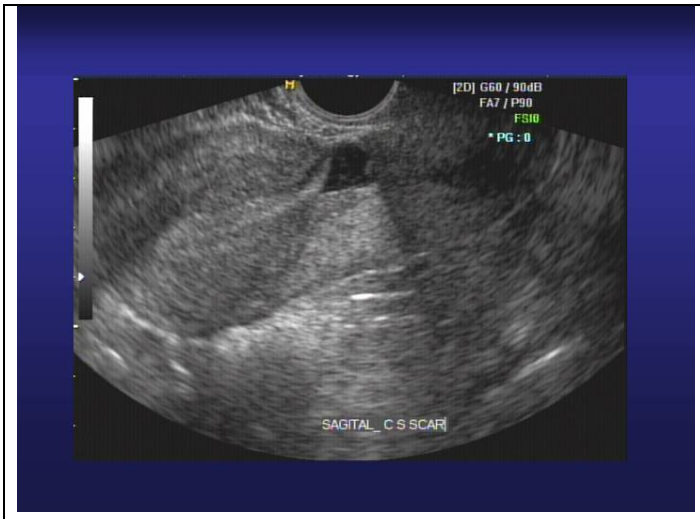
Lee et al. J Assist Reprod Genetics 2006;23:229-34

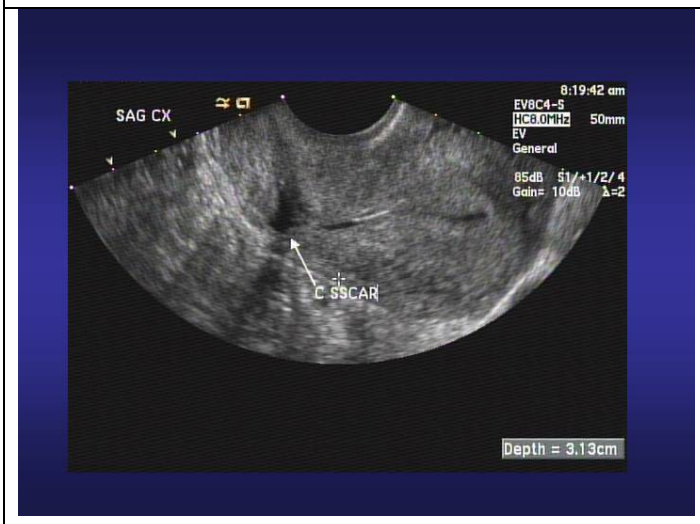
Cesarean Section Scar Defects or Diverticuli:

- Are seen more commonly after multiple cesarean sections.
- Are often low – below internal os.
- Lined by endocervical epithelium.
- Cause spotting, prolonged bleeding, discharge.
- Can be location of ectopic pregnancy.
- Can be surgically repaired.

Erickson and Van Voorhis. Obstet Gynecol 1999;93:802-5







Cesarean Section Scar Defects

- Can be associated with fluid in the endometrium.
- Cause could be excessive cervical mucus?
- We have anecdotally noted poor implantation rates with this condition.

Anecdotal Advice RE: Fluid IVF Cycle

- Fluid secondary to hydrosalpinges – aspirate at egg retrieval if still there at transfer – freeze embryos, remove hydrosalpinges before next cycle.
- Fluid secondary to PCOS or physiologic causes – leave it alone.
- Fluid secondary to cesarean section scar – aspirate – if still present at embryo transfer, freeze and repair defect.

Conclusions

- Ultrasound is a valuable screening tool in the infertility evaluation.
- Findings need to be interpreted with caution, as evidence for treatment leading to improved fertility is often scarce.

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NOTES

OVULATION INDUCTION AND OVARIAN HYPERSTIMULATION SYNDROME

Josef Blankstein, M.D., A.R.D.M.S.
Professor and Chairman
Department of Obstetrics and Gynecology
Rosalind Franklin University
The Chicago Medical School
Chicago, Illinois

LEARNING OBJECTIVES

At the conclusion of this presentation, participants should be able to:

1. List therapeutic measures available to induce ovulation.
2. Explain the role of ultrasound in monitoring ovulation induction.
3. Describe the role of ultrasound in preventing hyperstimulation.

Ovulation Induction and Ovarian Hyperstimulation Syndrome

Josef Blankstein, M.D., A.R.D.M.S.
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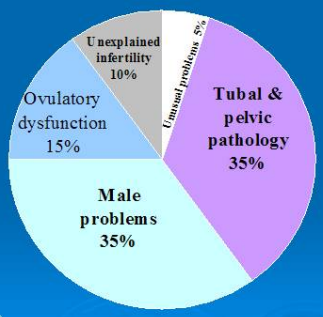
- List therapeutic measures available to induce ovulation.
- Explain the role of ultrasound in monitoring ovulation induction.
- Describe the role of ultrasound in preventing hyperstimulation.

DISCLOSURE

Josef Blankstein, M.D.

Nothing to disclose

Infertility Etiology



Speroff L, Fritz A (2005)

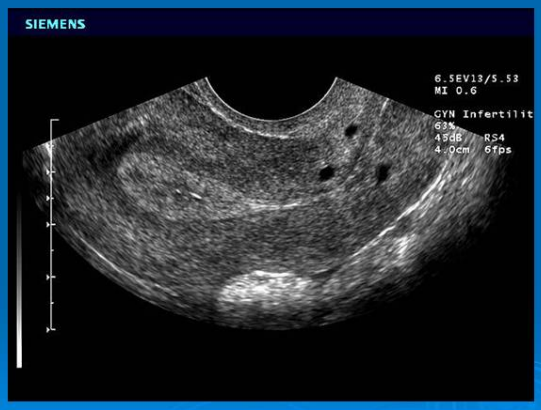
Ovulation Induction

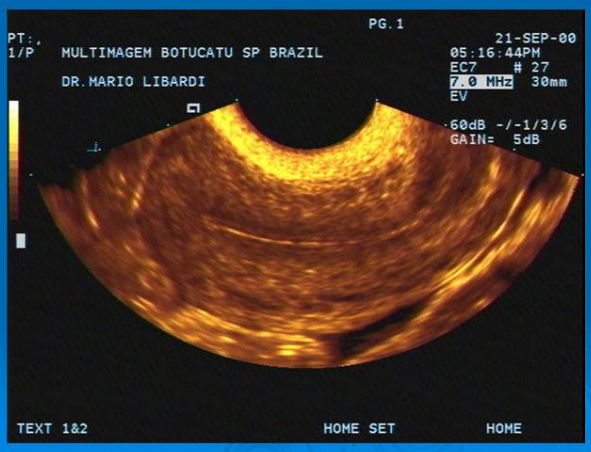
- May be needed for:
  - Patients with ovulatory dysfunction
  - Patients with unexplained infertility
  - Patients with tubal disease → I.V.F.
  - Patients with severe male problems → intracytoplasmic sperm injection (ICSI) following IVF

Anovulation- Treatment Options (Based on WHO classifications)

	Option I	Option II
Group I Low FSH	GnRH (pulsatile) Gonadotropins Bromocriptine	Gonadotropins, bromocriptine and clomiphene citrate
Group II Normal FSH	Clomiphene citrate	Gonadotropins Surgical approach
Group III High FSH	Ovum donation	

WHO = World Health Organization; FSH = follicle-stimulating hormone; GnRH = gonadotropin-releasing hormone





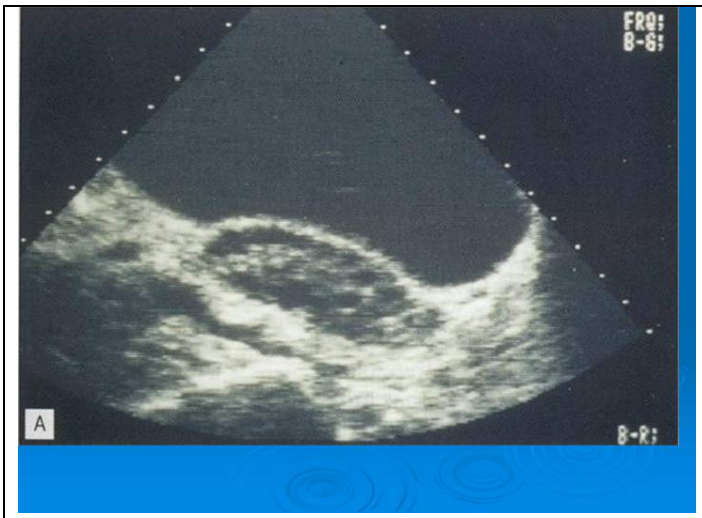
Clomiphene Citrate (CC): Mechanism of Action

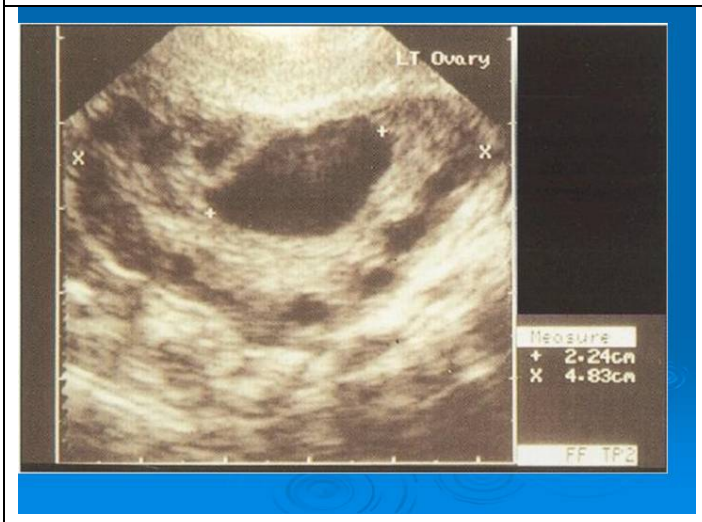
Primary site of action – central nervous system (CNS)

Binds to estrogen receptors in hypothalamus

Hypothalamus perceives hypoestrogenic state.

Pituitary increases release of gonadotropins.





Clomiphene-related Conceptions of Anovulatory Women with Polycystic Ovary Syndrome (PCOS)

- Restoration of ovulation in approximately 75%
- Pregnancies: 35%-40%
- The reason for discrepancy:
  - Anti-estrogenic effect of CC on endometrial development and cervical mucus

Homburg R. Hum Reprod 2005; 20: 2043-51

CC Ultrasound (US) Evaluation

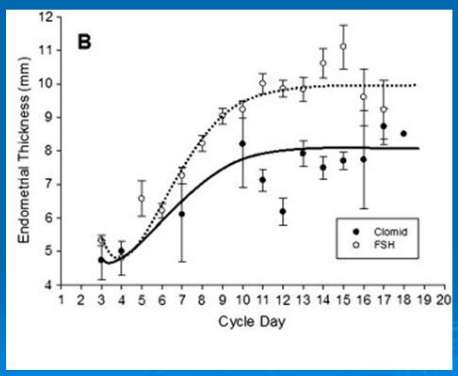
- US of follicular size and endometrial thickness on day 12-14
- It quickly identifies those not responding or who have depressed endometrial thickening.
- The added expense is justified by the prevention of protracted periods of ineffective therapy.

Homburg R. Hum Reprod 2005; 20: 2043-51

Defining the Proliferative-Phase Endometrial Defect

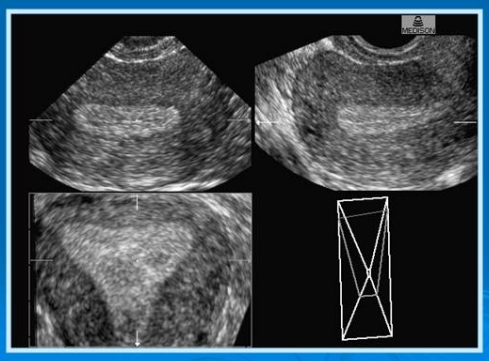
- Objective: To evaluate proliferative-phase development in a heterogeneous infertility population (n=246).
- Design: Retrospective study.

Bromer JG, Aldad TS, Taylor HS. Fertil Steril 2009; 91(3):698-704



Bromer JG, Aldad TS, Taylor HS. Fertil Steril 2009; 91(3):698-704

Endometrium



Defining the Proliferative-Phase Endometrial Defect

- Explanation for why CC is much more successful at inducing ovulation than resulting in ongoing pregnancy.
- Explanation for why there are lower pregnancy rates seen with using CC for superovulation than with gonadotropins.

Bromer JG, Aldad TS, Taylor HS. Fertil Steril 2009; 91(3):698-704

Comparison of Endocrine and Ultrasound Profiles During Ovulation Induction with Clomiphene Citrate and Letrozole in Ovulatory Volunteer Women

- Design: Prospective, randomized, double-blind, crossover study.

Jirge PR, Patil RS. Fertil Steril 2008 (epub)

Details of Preovulatroy Follicles Recorded during the Follicular Phase of Volunteer Normal Subjects during a Natural Cycle and Cycles Treated with CC

Cycles (n=30)	Number of follicles on day of LH Surge
Natural cycles N=15	1.0
CC cycles N=15	1.50 ± 0.15 (1.2 - 1.8)
P value	.003

Jirge PR et al. Fertil and Steril 2008

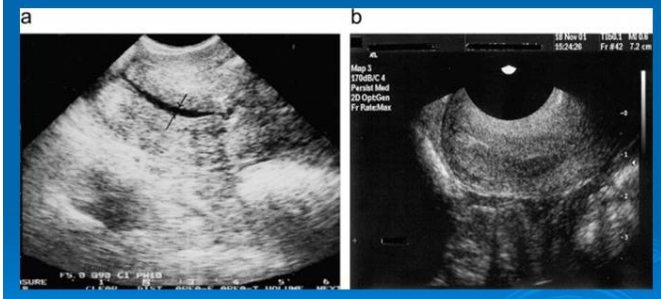
LH = luteinizing hormone

Comparison of the Physiological Parameters Recorded during Treatment of Volunteer Subjects during a Natural Cycle and Cycles Treated with CC

Table 2 Cycles (n=30)	Follicular phase length (days)	Endometrial thickness on day 0 (mm)	Endometrial thickness midluteal phase (mm)
Natural N=15	14.0 ± 0.5 (12.9-15.0)	8.5 ± 0.3 (8.0-9.0)	9.6 ± 0.3 (8.9-10.2)
CC N=15	13.9 ± 0.3 (13.2-14.5)	7.6 ± 0.3 (7.1-8.2)	9.1 ± 0.4 (8.4-9.8)
P value	.80	.015[a]	.29

Jirge PR. Ovulation induction with clomiphene and letrozole. Fertil and Steril 2008

(a) Cervical canal measurement near ovulation and (b) after ovulation



Wolman I et al. Fertil and Steril 2009

Cervical Score Below and Above Cervical Canal Diameter of 1 mm

Canal diameter	Low score (≤5; n=52)	High score (>5; n=49)	*P*
≤ 1 mm	42 (84)	8 (16)	
> 1 mm	10 (19.6)	41 (80.4)	< .001

Note: Data in parentheses are percents

Wolman I et al. Fertil and Steril 2009

Relationship Between Endometrial and Subendometrial Blood Flow and Pregnancy after Intrauterine Insemination

- Methods:
  - Blood flow parameters measured using 3-D power Doppler
- Design: Prospective study

Ari Kim, MD, et al. Fertil and Steril May 2009

Relationship Between Endometrial and Subendometrial Blood Flow and Pregnancy after Intrauterine Insemination

- Main outcome measures: Vascularization index (VI), flow index (FI), and vascularization flow index (VFI) of the endometrium, as well as those of subendometrial region.
- These measurements were analyzed in relation to IUI outcome pregnant vs. non-pregnant.

Ari Kim, MD, et al. Fertil and Steril May 2009

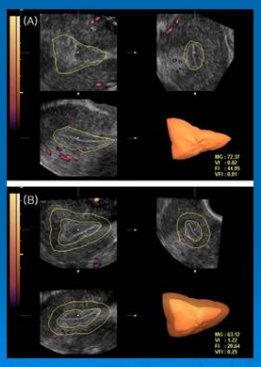
Relationship Between Endometrial and Subendometrial Blood Flow and Pregnancy after Intrauterine Insemination

- Results:
  - The pregnant group had higher endometrium VI, FI and VFI scores than the non-pregnant group.
  - The subendometrial region VI, FI and VFI scores did not differ between the groups .

Ari Kim, MD, et al. Fertil and Steril May 2009

Three-Dimensional Power Doppler Images Generated Using VOCAL Software.

Endometrial



VOCAL = virtual organ computer-aided analysis

Subendometrial blood flow parameters on the day of IUI

Kim, Endometrial blood flow in IUI. Fertil and Steril 2009.

Persistent Clomiphene Failure

Ovulation
↓
No conception
↓
Superovulation / IUI
or
in vitro fertilization

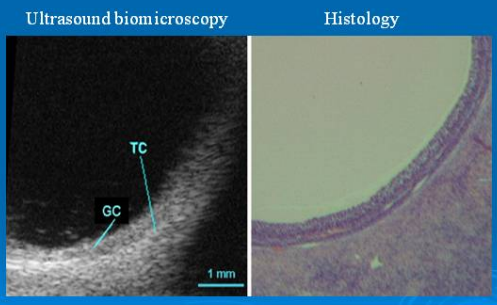
No ovulation
↓
Laparoscopic induction of ovulation
↓
Gonadotropins

Principles of Gonadotropic Therapy

- FSH - Recruitment selection
- LH - Stimulation of theca cells

→ Androgens → Estrogens

Antrum, Granulosa (GC), and the Theca Cells (TC) in a Preovulatory Follicle



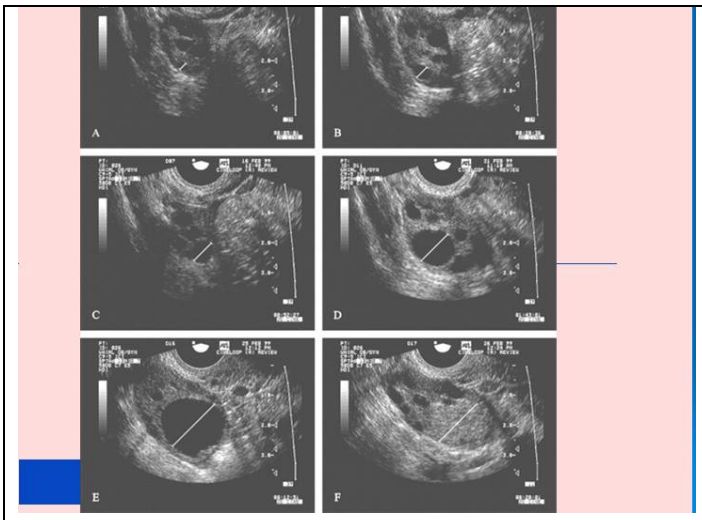
Pallares et al, Fertil-Steril 91;622,-2009

Growth Rates of Ovarian Follicles during Natural Menstrual Cycles, Oral Contraception Cycles and Ovarian Stimulation Cycles

OBJECTIVE: To compare growth rates of ovarian follicles during natural menstrual cycles, oral contraception cycles and ovarian stimulation cycles using standardized techniques.

DESIGN: Prospective, comparative, observational, longitudinal study

Baerwald,et al. Fertil and Steril, 2009



Comparison of Mean Follicular Growth Rates in Natural Menstrual Cycles and Ovarian Stimulation Cycles

		N	Growth rate (mm/day)
Natural menstrual cycles	Total	181	1.42 ± 0.05[a]
Ovarian stimulation cycles	Total	794	1.69 ± 0.02[b]

Mean Follicular Growth Rate

- 1.4 mm/day in spontaneous menstrual cycles
- 1.7 mm/day during ovarian stimulation cycles
- Continued research on the effects of greater follicular growth rates and shorter intervals to ovulation

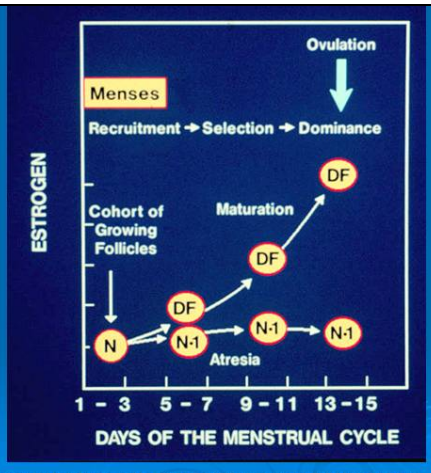
Baerwald et al. Fertil and Steril (2009)

Monitoring of Gonadotropic Therapy

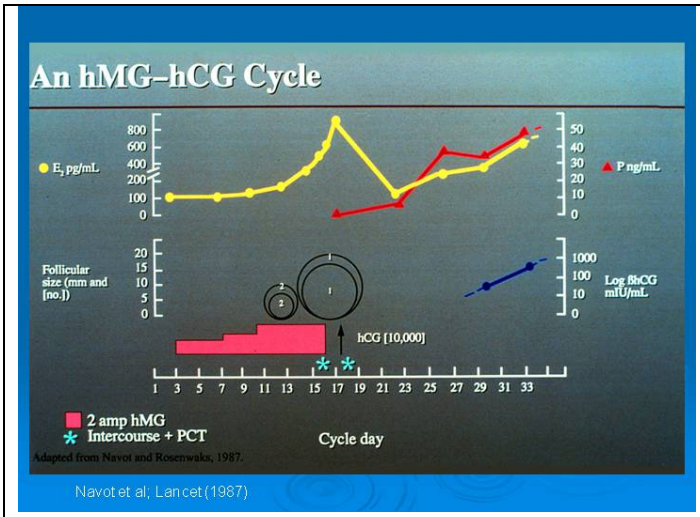
- The dose that is effective in evoking ovarian response
- Length of time required for follicular maturation
- The appropriate time for hCG administration

Gonadotropin Starting Dose

- Age
- FSH
- Antral follicle count
- Response to initial ovulation trial



Hodgen G. Ovarian physiology and In Vitro Fertilization in ovulation induction (Edited Collins R.C) Springer Verlag (1990) 22-40



Navot et al; Lancet (1987)

Ovarian Follicle Monitoring

- Initially – only estradiol (E_2)
- Since 1979, ultrasound has also been included.

1979: Hackeloer BJ *et al.*
Am J Obstet Gynecol 135:122–128


B-J Hackeloer

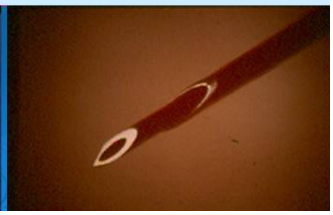
First paper about ovarian follicles seen by ultrasound

30 years ago

Since then....

Routine US scan during infertility treatment include only:

Follicle tracking (number and diameter)



We Need Better Prognostic Tools To Evaluate the Chance To Conceive !

Single embryo transfer is being adopted by many centers, especially for the younger patient.

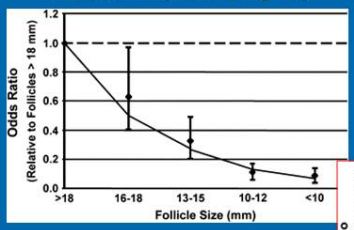
Try to identify the follicle/embryo with the greatest potential for pregnancy.

A Quantitative Assessment of Follicle Size on Oocyte Developmental Competence

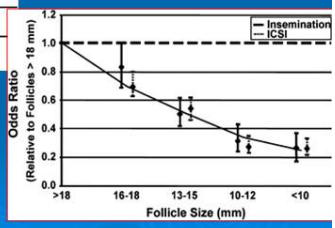
DESIGN: Prospective study

Rosen et al. Fertil and Steril; Vol 90: 2008

The odds of aspiration of metaphase II oocytes relative to the lead (>18 mm) follicular group



The odds of fertilization relative to the lead (>18 mm) follicular group using all retrieved cumulus oocyte complexes and stratified by method of fertilization



Rosen,et al; Fertil and Steril; Vol 90: 2008

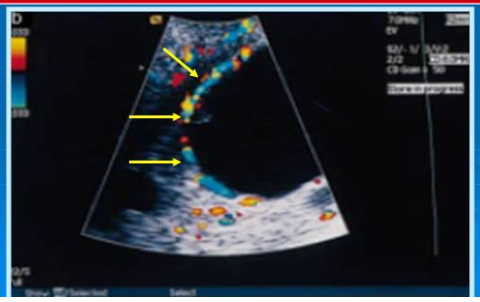
A Quantitative Assessment of Follicle Size on Oocyte Developmental Competence

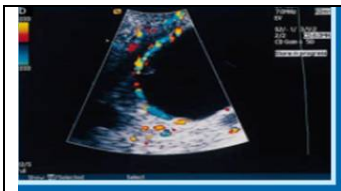
The results demonstrated that the odds of oocyte maturation and fertilization rate were statistically significantly decreased with smaller follicles.

Fig 1and 2 – Rosen. Follicle size and oocyte developmental competence. Fertil and Steril 2008

A Marker To Assess Quality of Ovarian Follicles

Peak systolic velocity (PSV) measured in the follicular wall



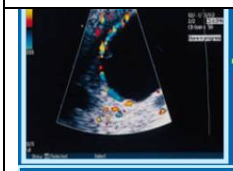


Color Doppler indices of follicular blood flow as predictors of pregnancy after IVF and ET .
Coulam *et al.* Hum. Reprod. 1999

In fact…

Aspiration of these follicles
[PSV > 10 cm/s]
resulted in increased:

- **Oocyte recovery**
- **Fertilization rate**
- **Embryo quality**



Coulam *et al.* Hum. Reprod. 1999

Amount of Visible Color Flow Around the Follicle

grade 1: ¼ of the follicle surrounded by color signals
grade 2: ½ surrounded by color signals
grade 3: ¾ surrounded by color signals
grade 4: **entire follicle** surrounded by color signals

Results (IVF)

Clinical pregnancies: 11/106 (10%)
More pregnancies: **PSV >10 cm/s** (day hCG)

All pregnancies resulted from follicles **grade 3 or 4**

Coulam, Hum. Reprod., 1999; 14: 1979 - 1982

Study: Associations between follicular blood flow, oocyte recovery, and pre-implantation embryo quality.

Nargund G *et al. Hum. Reprod.*, 11, 109–11, 1996

PSV > 10 cm/s : 70% chance of good-quality embryos

< 10 cm/s : 14% chance of good-quality embryos

Conclusion:
PSV is a good marker indicating follicular quality!

2

New Sonographic Parameters

Power Doppler flow

"Color Doppler angio"

Up to 5 times more sensitive in detecting blood flow than color Doppler, especially in low blood flow

Moving to 3D…

In 2-dimensional studies, we assess blood flow of single ovarian vessels...

In 3D - power Doppler, we evaluate total blood supply to the whole organ

2D → 3D

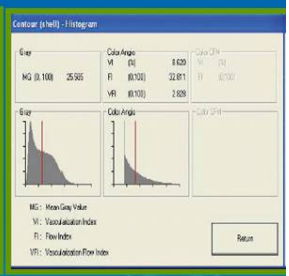
Single vessel → Whole organ

3 Power Doppler Parameters

Vascularization index (VI)
Percent of vessels in the tissue (%)

Flow index (FI)
Average intensity of flow (range 0…100)

Vascularization-flow index (VFI)
A feature of both vascularization and flow (range 0…100)



For safety perspective see reference; Abramowicz et al; Barnett, et al; Bly, et al; Hershkovitz et al.Sheiner, et al.

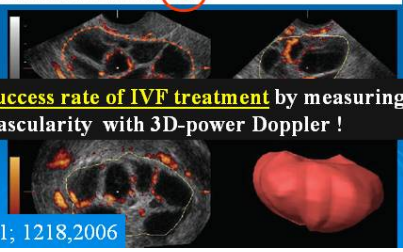
Human Reproduction Vol.21, No.5 pp. 1218–1226, 2006
Advance Access publication January 12, 2006.
doi:10.1093/humrep/del471

Assessment of the ovarian volume, number and volume of follicles and ovarian vascularity by three-dimensional ultrasonography and power Doppler angiography on the HCG day to predict the outcome in IVF/ICSI cycles

Luis T.Mercé[1,2], Santiago Bau[1], María J.Barco[2], Juan Troyano[3], Rosina Gay[4], Florencia Sotos[4] and Amelia Villa[4]

[1]Assisted Reproduction Unit, International Ruber Hospital, Madrid, [2]University Clinic "Lozano Blesa", Zaragoza, [3]University Hospital in La Laguna, Tenerife and [4]IVF Laboratory, International Ruber Hospital, Madrid, Spain

PROSPECTIVE STUDY



Predicting the success rate of IVF treatment by measuring ovarian vascularity with 3D-power Doppler !

Human Reproduction, 21; 1218,2006

Table III. Three-dimensional ultrasonography and power Doppler angiography parameters on the HCG day in relation to IVF/ICSI outcome

	Pregnant (n = 38)	Non-pregnant (n = 42)	P
Ovarian volume (ml)	62.89 ± 21.31	51.37 ± 21.22	0.020
Number of follicles	14.39 ± 6.28	11.71 ± 6.28	0.070
Total follicular volume (ml)	35.76 ± 11.60	30.14 ± 11.76	0.035
Vascularization index	24.73 ± 8.11	18.44 ± 10.25	0.003
Flow index	68.65 ± 8.39	62.20 ± 9.93	0.003
Vascularization flow index	8.82 ± 3.15	6.44 ± 3.75	0.003

Data are presented as mean ± standard deviation.

RESULTS
VI, FI, VFI were significantly greater in the pregnant group

Human Reproduction, 21; 1218,2006

Power Doppler Assessment of Follicle Vascularity at the Time of Oocyte Retrieval in in Vitro Fertilization Cycles

Objective: To assess the practicality of using power Doppler (PD) to assess follicular vascularity at the time of oocyte retrieval.

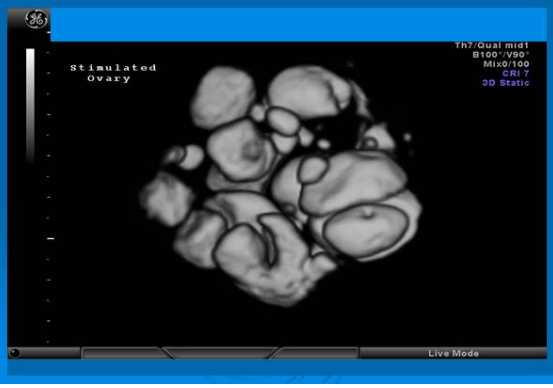
Design: Prospective study.

Robson et al. Fertil and Steril 2008

Results

Pregnancy rates when the embryo transfer cohort contained at least one embryo from a highly vascular follicle were 50% vs. 15.4%

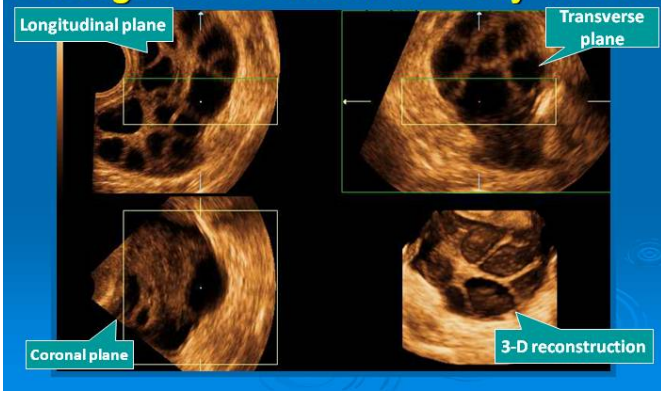
3D of Stimulated Ovary



Sono-AVC (Automatic Volume Calculation)

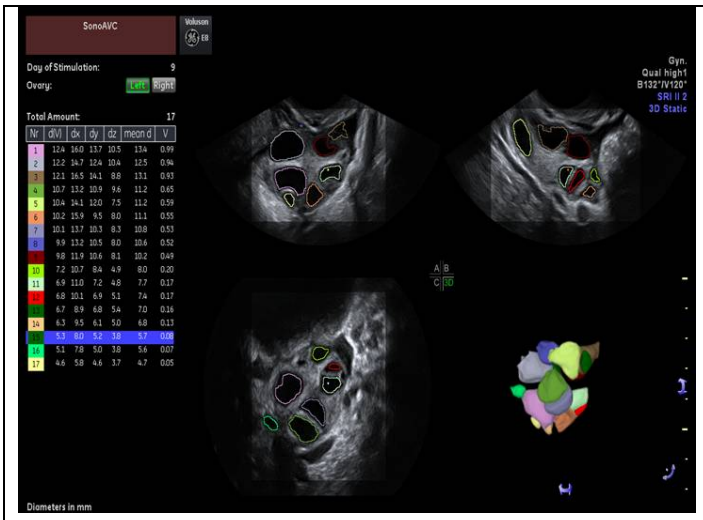
- A new software program (GE) within a 3-D data set→ automatic estimation of diameter and volume
- Each volume is separately color-coded.

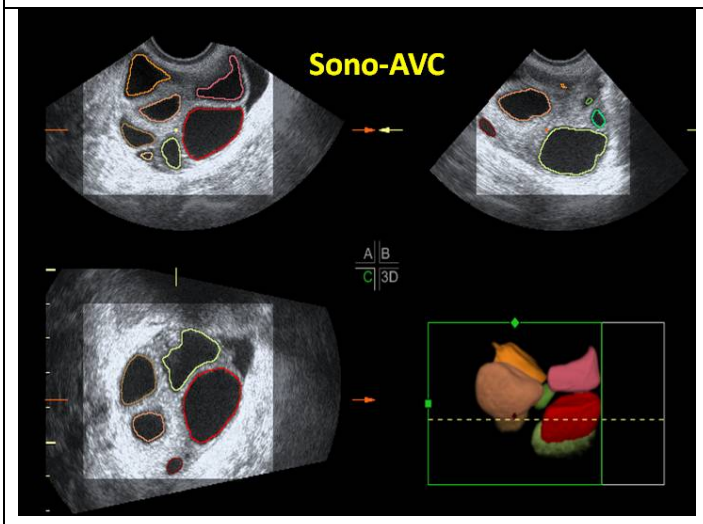
3D US Reconstruction and Multiplanar View of the Ovary During ART Treatment - Day of hCG



Sono-AVC

- Care should be taken that the region of interest (ROI) is large enough to encompass the entire ovary.
- Once the ROI is accepted, the ultrasound program will automatically identify the ovarian follicle and the volumetric parameters for each follicle





Automated Measurements of Follicle Diameter a Chance to Standardize?

- Automated measurement of follicular diameters using the AVC was compared to manual measurements from 2-D and 3-D ultrasound.
- Sono-AVC provides measurements that are more accurate than manual measurements.
- Time taken for measurements was significantly shorter

Raine-Fenning, Fertility and Sterility 2009

Complication of Gonadotropic Therapy

Ovarian hyperstimulation

Multiple pregnancy

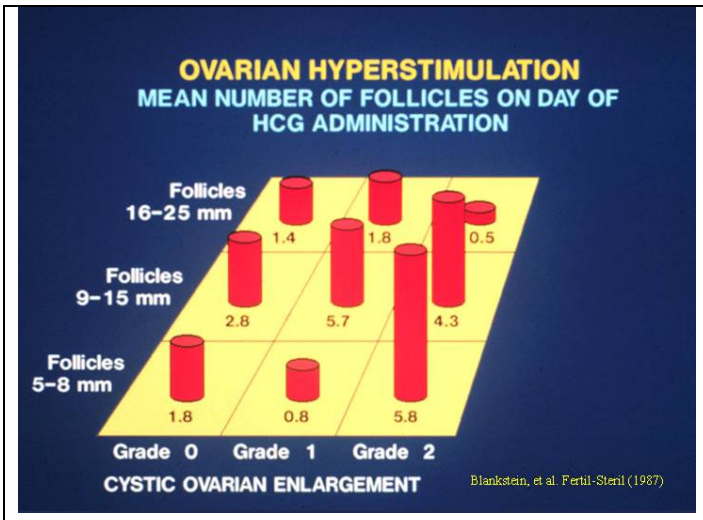
Ovarian Hyperstimulation Syndrome (OHSS)

- Enlarged cystic ovaries
- Increased in capillary permeability
- Ascites
- Hydrothorax
- Hypovolemia
- Thromboembolic phenomena

Ovarian Hyperstimulation Study

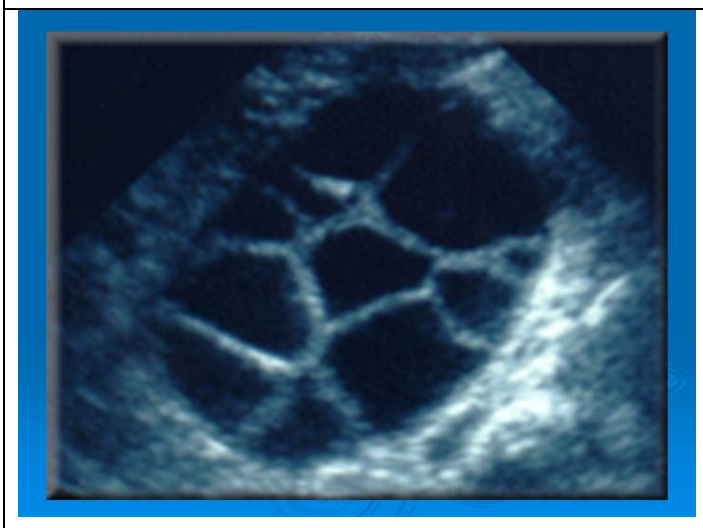
- Prospective study - protocol
- hMG- Individually adjusted dose
- hCG- based on estradiol levels
- Ultrasound scanning, during follicular phase until the day of hCG
- The number and size of the ovarian follicles were evaluated

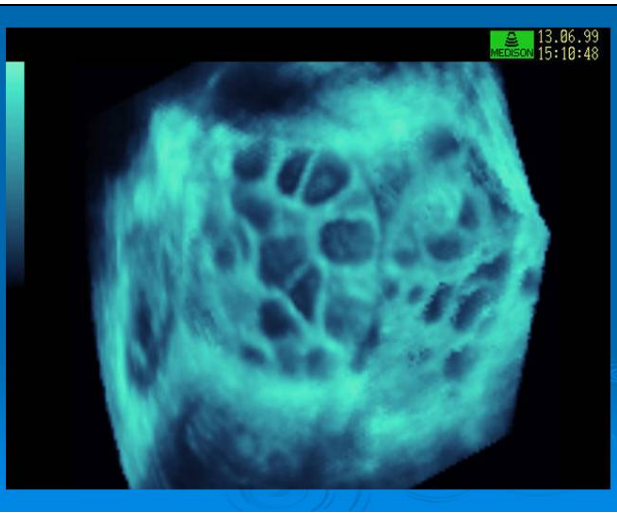
Blankstein et al. Fertil Steril



Ovarian Hyperstimulation

- Specific preovulatory follicular configuration characterizes women prone to develop mild and severe hyperstimulation.
- hMG should be interrupted in the presence of multiple preovulatory follicles, especially if most of them are immature (less than 9 mm).





Can Quantitative 3-D Power Doppler Angiography Be Used To Predict Ovarian Hyperstimulation

Objective:

- To test the hypothesis that **ovarian vascularity** is increased in women developing OHSS
- To assess its **predictive value**

Design: Prospective observational study

K. Jayaprakasan, et al (J.Raine-Fenning Group: Ultrasound Obstet Gynecol 2009; 33:583-591

Can quantitative 3-D power Doppler angiography be used to predict ovarian hyperstimulation

- Methods
  - N=118
  - Antral follicle count, ovarian volume, and ovarian vascularity flow index and vascularization flow index were compared between OHSS and control groups. Multiple regression analysis were used.

K. Jayaprakasan, et al (J.Raine-Fenning Group: Ultrasound Obstet Gynecol 2009; 33:5833-591

Can quantitative 3-D power Doppler angiography be used to predict ovarian hyperstimulation

- Conclusion:
  - Women developing OHSS during IVF do not demonstrate an increased ovarian blood flow as measured by 3-D.
  - OHSS patients have a significantly higher antral follicle count

K. Jayaprakasan et al. (J Raine-Fenning Group: Ultrasound Obstet Gynecol 2009; 33:583-591

The Role of E_2 vs. US: Cochran Database

There is no evidence from randomized trials to support cycle monitoring by ultrasound plus serum estradiol as more efficacious than cycle monitoring by ultrasound only on outcomes of live-birth and pregnancy rates.

Kwan, I. Bhattacharya et al. (Systemic Review) Cochrane Mentrual Disorders and Subfertility Group Cochrane Database of Ststemic Reviews. 4, 2008

The role of E_2 vs. US

- As far as OHSS, randomized trial with a sufficiently large sample is needed.
- Until such a trial is considered, ultrasound plus serum estradiol may need to be retained as a precautionary good practice point.

Kwan, I. Bhattacharya, et al (Systemic Review) Cochrane Mentrual Disorders and Subfertility Group Cochrane Database of Ststemic Reviews. 4, 2008

Summary

- Ultrasound is an essential part of monitoring ovulation induction.
- Various methods to assess follicular vascularity are available.

Summary

- Since single embryo transfer is the trend, more studies are needed to identify the "best" follicle with the greatest potential for pregnancy.
- Ultrasonography can assist in reducing the occurrence of hyperstimulation.

Thank you

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NOTES

ULTRASOUND DIAGNOSIS OF UTERINE ANOMALIES AND THEIR EFFECTS ON FERTILITY

Alex Hartman, M.D.
True North Imaging
Thornhill, Ontario, Canada

LEARNING OBJECTIVES

At the conclusion of this presentation, participants should be able to:

1. Describe the ultrasound modalities used to diagnose uterine anomalies.
2. Assess the use of 3-dimensional (3D) ultrasound to diagnose uterine malformations.
3. Classify uterine anomalies.
4. Decide when the use of 3D sonohysterography should be recommended.

Ultrasound Diagnosis of Uterine Anomalies and Their Effects on Fertility

Alex Hartman, M.D.

True North Imaging, Thornhill, Ontario, Canada

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Disclosure

Nothing to disclose

Diagnosis of Uterine Malformations

Different Modalities

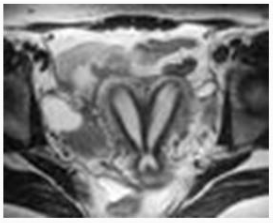
- Hysterosalpingography
- Hysteroscopy
- Magnetic resonance imaging (MRI)
- Ultrasound

Hysterosalpingogram (HSG)

Hysteroscopy

Uterine Malformations

MRI



Ultrasound Modalities

1. 2-dimensional (2D) ultrasound
2. Sonohysterography
3. 3D ultrasound
4. 3D sonohysterography

Sonohysterography (SHG)

An ultrasound technique in which the endometrial cavity is distended with saline, allowing evaluation of the single layer of the endometrium and uterine cavity.

Normal Uterus

SHG to Differentiate Uterine Anomalies

20 patients with recurrent fetal loss (RFL) and HSG diagnosis of uterine anomalies had SHG that correctly differentiated the patients with bicornuate uteri and those with septate uteri.

Alborzi, Fertil Steril 2002;78:176-178.

3D Ultrasound

3D ultrasound is playing an increasingly important role in ultrasound development. It involves a real-time capability to build and store a volume of ultrasound data, and display it in various ways.

Prevalence ?

Reasons for confusion –

1 – Different methods of diagnosis
2 – Widely variable historical data
3 - Inaccurate diagnoses of müllerian anomalies

Prevalence ?

Prevalence of müllerian duct anomalies detected at ultrasound

- Transabdominal (TA) and transvaginal (TV) study
- 2,065 consecutive females (aged 8-93 years)
- 8 anomalies (septate, bicornuate)

PREVALENCE – **1/250**

Byrne, Am J of Medical Genetics, 2000

3D US for the Assessment of Uterine Anatomy and the Detection of Congenital Anomalies

61 Patients with RFL or infertility were investigated with 3D ultrasound

- Normal uterus 72%
- Arcuate 15%
- Major defect 5%
- Poor 3D (fibroids) 8%

Jurkovic D et al. Ultrasound Obstet Gynecol 1995;5:233-7

Detection of Congenital Müllerian Duct Anomalies (MDA) Using 3D US

-40 Patients with RFL or infertility evaluated with 3D US and then reassessed with laparoscopy and/or hysteroscopy

28 Patients with MDA
12 Normal

3D sensitivity and specificity both - 100%

Wu, J Clin Ultrasound 1997;25:487-492

Septate Uterus: Detection by Different Forms of Ultrasound

- 420 infertile patients

  278 patients had a septate uterus confirmed hysteroscopically

	Sensitivity(%)	Specificity(%)	PPV(%)	NPV(%)
3D	98.38	100	100	96.00
SHG	98.18	100	100	95.45

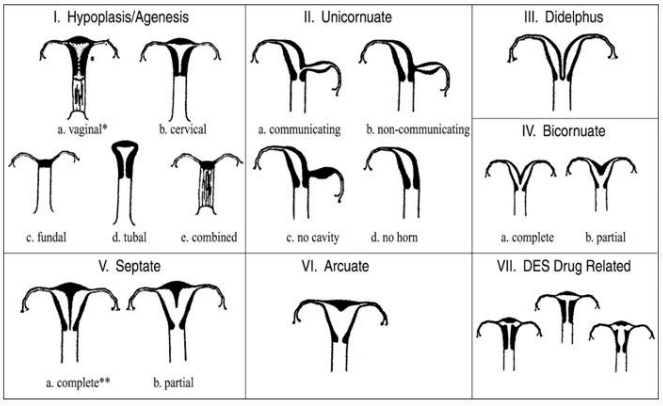
Kupesic and Kurjac, JUM 1998;17:631-636

PPV = positive predictive value
NPV = negative predictive value

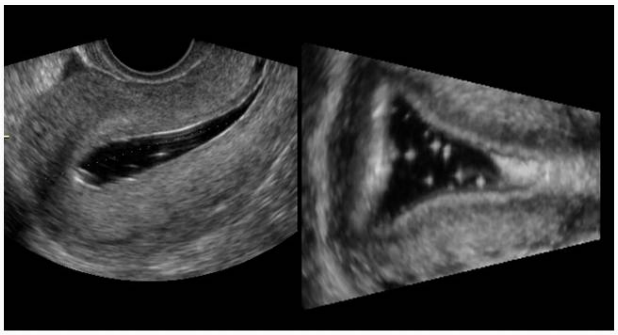
Prevalence

1. 1/250 – **0.4%**
2. 278/420 - **66.2%**
3. Various **3% - 4%**

What is the real prevalence?
Which methods are best for diagnosis?
How do you classify uterine anomalies?



Normal 3D/4D - Sonohysterogram



A Slightly Modified ASRM Classification

- **Arcuate** – Endometrial indentation < 1 cm. No serosal cleft. Normal cervix.
  - Ratio of the height of fundal indentation of the cavity to the distance between the horns > 0.1 (Sorensen SS, AJOG 1983; 145:659)
- **Septate** – Endometrial indentation, usually >1 cm. If septum extends to lower uterine segment it is considered complete. Fundal cleft, if present, < 1 cm. Cervix may or may not be divided.
- **Bicornuate/Didelphys** – Divergent cornua separated by a fundal cleft of > 1 cm. Bicornuate has a connection between the horns.

Prospective Study

- Sonohysterography vs. 3D ultrasound for the diagnosis of uterine anomalies: A prospective blinded study of 1000 consecutive women

Prospective Study

- [1]Hartman A, [1]Hartman J, [1]Hartman M, [2,3]Tur-Kaspa I.
- [1]True North Imaging, Thornhill, Canada,
- [2] IVF Unit, Barzilai Hospital, Ben-Gurion University, Ashkelon, Israel and
- [3]Reproductive Genetics Institute, Chicago, IL, USA

Aim

To investigate, as a prospective blinded study, the accuracy of sonohysterography (SHG), compared to three-dimensional ultrasound (3D US), in detecting uterine anomalies. The prevalence of uterine anomalies was also assessed.

Method

- 1000 consecutive women underwent SHG.
- 591 were referred because of infertility.
- 409 were referred for the investigation of irregular uterine bleeding or abnormal endometrial appearance.
- In addition, all underwent 3D US for the diagnosis of uterine anomalies.

Results

- **239** of the **1000** women were diagnosed by 3D US to have uterine anomalies.
- Arcuate uterus was the most frequent anomaly **(n=186)** and the others were partial **(n=25)** or complete **(n=20)** septate, bicornuate **(n=2)**, didelphys **(n=1)**, unicornuate**(n=1)**, hypoplastic **(n=1)**, septate/arcuate **(n=3)**.
- The prevalence of anomalies was significantly higher in the infertile group ***(29.8%)*** compared to the non-infertile group (***15.4%;*** chi-square = 27.47, $p < .0001$).

Infertile Patients (n = 591)

Type of Malformation	3D	SHG
Normal	415 (**70%**)	473 (80%)
Arcuate	137 (**23%**)	86 (15%)
Septate*	36 (**6%**)	16 (3%)
Others	3 (**<1%**)	2 (<1%)

*includes subseptate

Statistical Analysis

Sensitivity, specificity, positive and negative predictive powers of SHG compared to 3D US, as the gold standard, were measured.

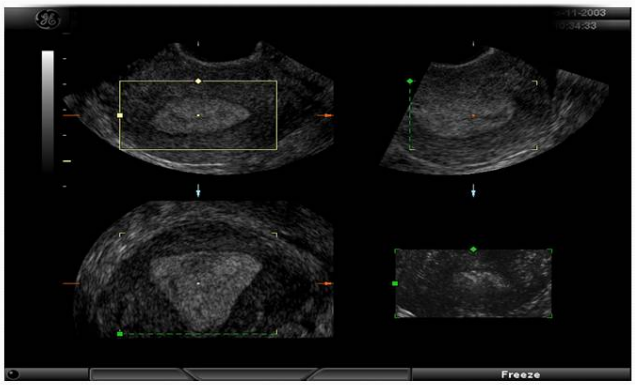
Results

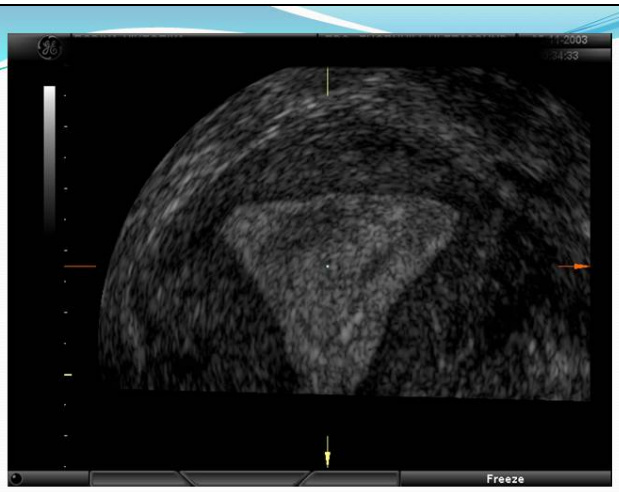
	Sensitivity	Specificity	Positive P. V.	Negative P. V.
Infertile	**61.9**	**97.8**	**92.4**	**85.8**
Fertile	**57.1**	**99.1**	**92.3**	**92.7**

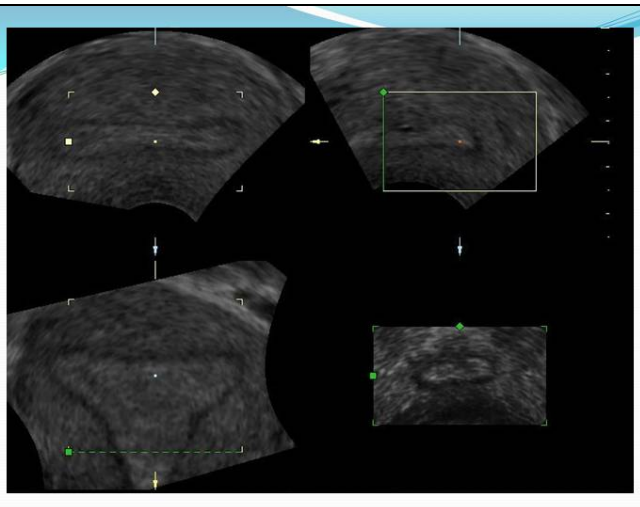
Conclusions

- SHG diagnosed most uterine anomalies.
- When uterine anomaly is suspected, 3D US may be recommended.
- 3D US allows precise recognition of uterine anomalies by visualizing both the uterine cavity and the fundal uterine contour
- 3D US should become the gold standard for diagnosing uterine anomalies instead of hysteroscopy or hysterosalpingogram with laparoscopy.

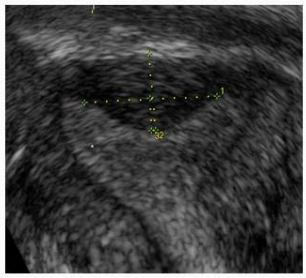
Normal Cavity





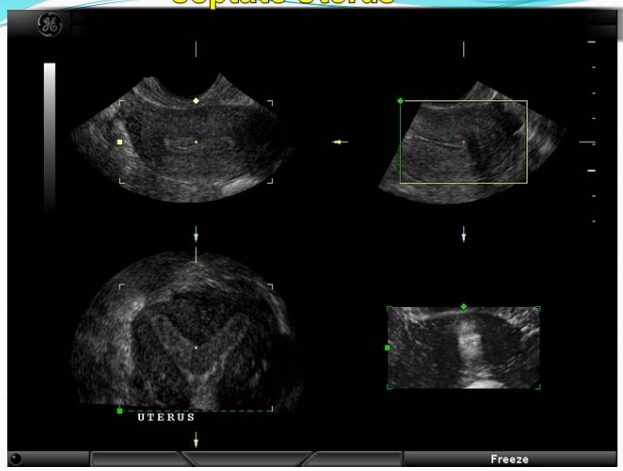


Arcuate Uterus

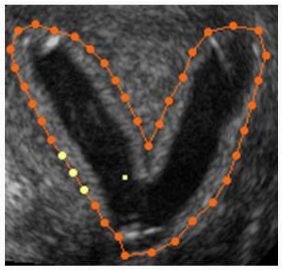


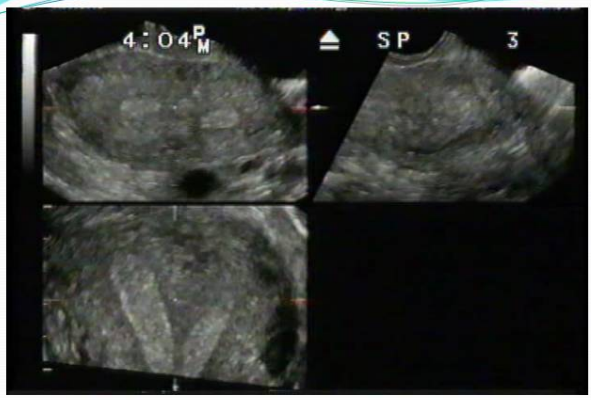
Arcuate 3D Sonohysterogram

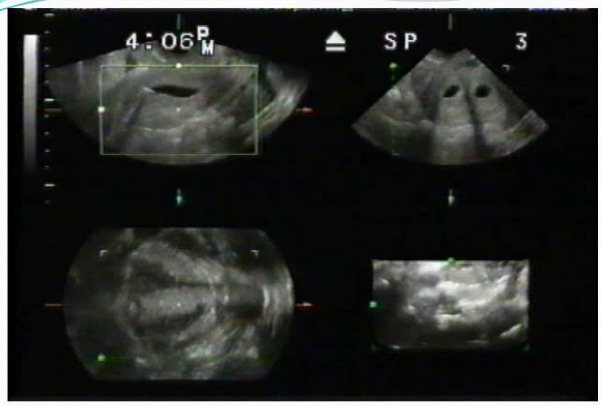
Septate Uterus



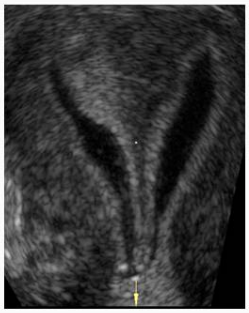
3D Sonohysterogram - Septum



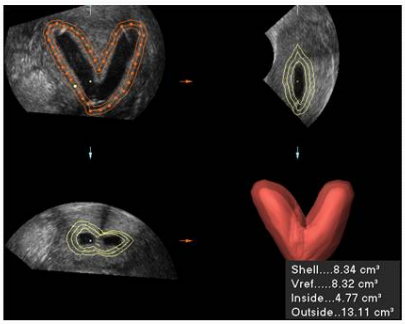




Septum 3D Sonohysterogram



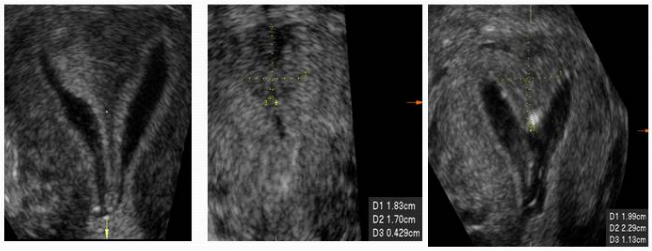
3D Sonohysterogram and Septal Volume



Septal Volumes

- Now are being assessed prior to and post-surgery in all patients, especially in those with recurrent fetal loss (RFL)
- 2 studies underway to correlate the degree of repair and residual septal volume to subsequent pregnancy

3D and 3D Sonohysterography



3D Ultrasound vs. 3D Sonohysterography in the Diagnosis of Uterine Anomalies

Michael Hartman, MD, Jason Hartman, BA, Brian Hartman, Carmen Oprea, MD, and Alex Hartman MD

Department of Obstetrics and Gynecology, Memorial University of Newfoundland, St. John's, Newfoundland, Canada
True North Imaging, Thornhill, Ontario, Canada

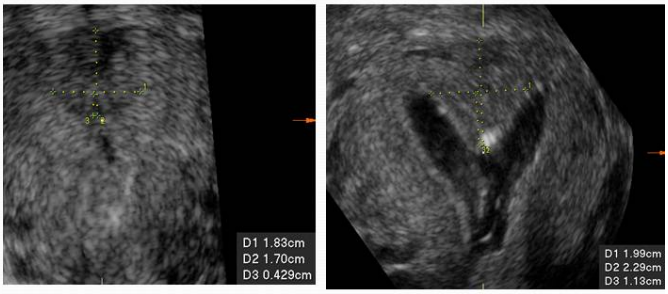
Materials and Methods

- 600 consecutive patients being investigated for infertility from the greater Toronto area were referred for investigation
- Each patient had both 3D US and 3D SHG, with the procedures being done on separate visits in the same cycle
- SHGs were performed by a physician with extensive experience with the procedure

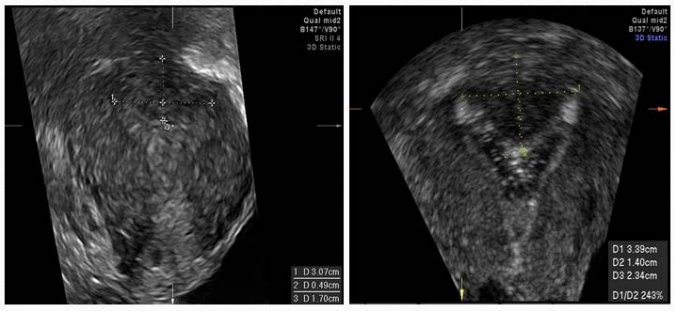
Results

	3D US (n=600)	3D SHG (n=600)
Arcuate	18.7% (112)	28.3% (170)
Borderline arcuate/partial septum	1.8% (11)	1.8% (11)
Partial septum	1.5% (9)	2.2% (13)
Complete septum	1.2% (7)	1.7% (10)
Bicornuate	0	0.2% (1)
Total	23.2% (139)	34.2% (205)

3D and 3D Sonohysterography

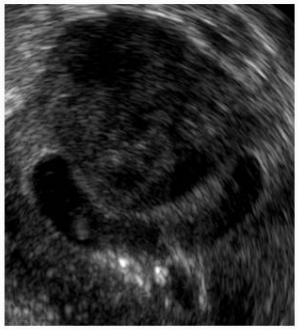


3D and 3D Sonohysterography

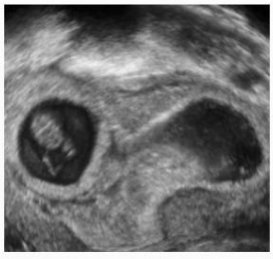


What Is This?

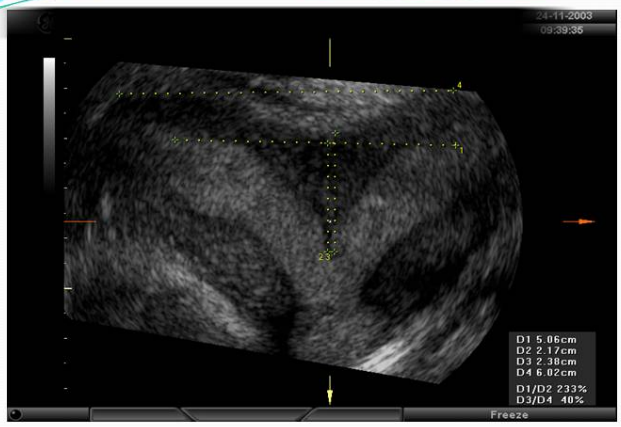
Another Septum?



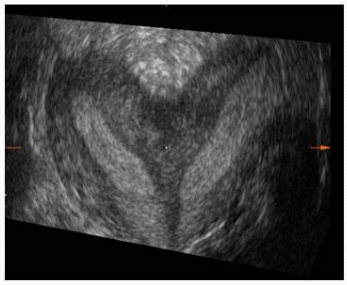
Pregnancy in Septate Uterus

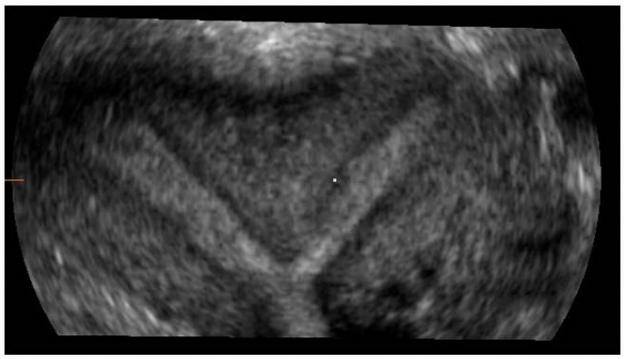


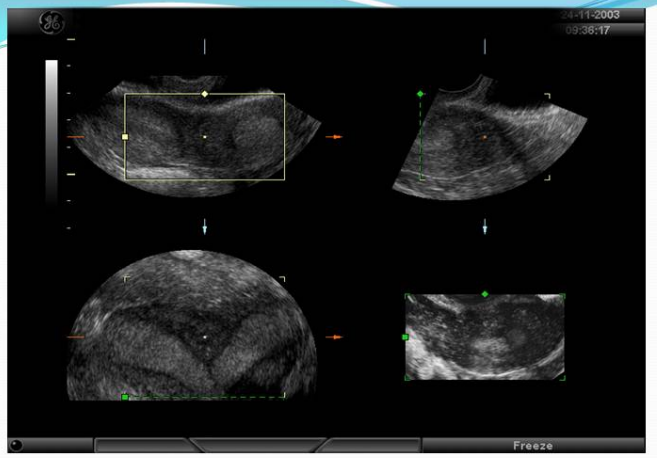
Bicornuate Uterus



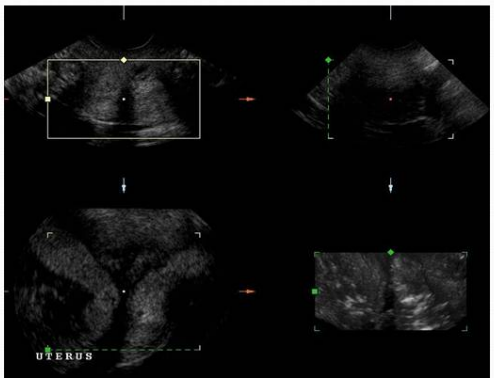
Bicornuate

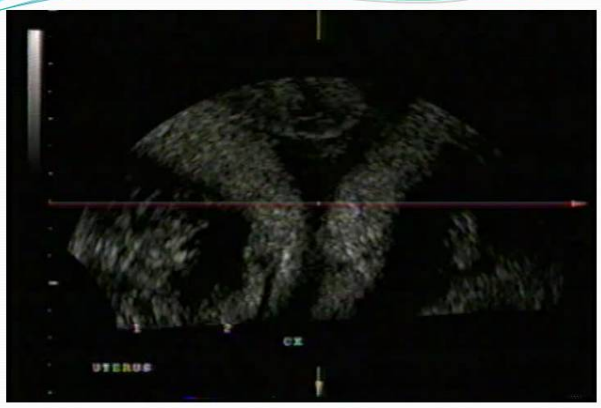






Uterus Didelphys




UTERUS
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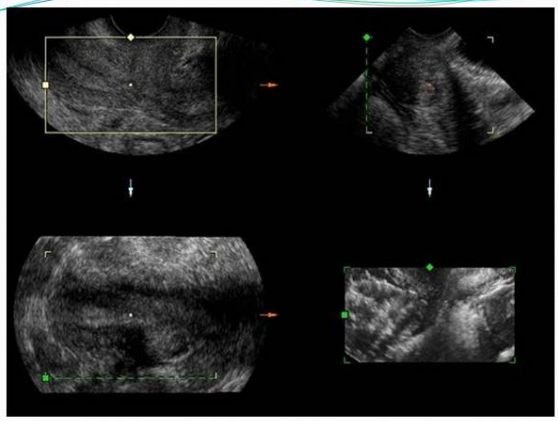
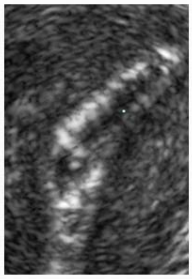


31-Year-Old Patient – Unicornuate, No Right Kidney or Ovary



Left Unicornuate with Right Rudimentary Horn

T – Shaped Uterus

Pregnancy Outcome

- 12 patients with complete septations and pregnancies
  - 4 survived – implantation on lateral walls
  - 8 miscarried –
    - 6 – septal implantation
    - 1 - mixed implantation
    - 1 - undetermined

Fedele, AJR, 1989

Pregnancy Outcome

- Müllerian defects in women with normal reproductive outcome
  - 22/679 had Müllerian defects (**3.2%**)
    - 90 % septate uteri
    - 5 % bicornuate

5 % unicornuate

Conclusion

Based on this study, the usefulness of septum resection in patients with no previous reproductive failure should be questioned.

Simon, Fertil Steril, 1991

Counterpoint - Why Look for a Septum?

"The experts were almost unanimous in their opinion that subseptate uterus requires surgical correction even in women who have not suffered recurrent pregnancy loss."

Jurkovic, *UOG*, 2007

Müllerian Duct Anomaly Prevalence

Retrospective study

3181 patients

Overall prevalence – **4%**

Infertile patients – **6.3 %**

Fertile patients - **3 %**

Raga, Human Reproduction, 1997

Live-Birth Rates

Normal (No MDA)	**83% - 85%**
Arcuate	**83%**
Bicornuate	**62.5%**
Septate	**62%**
Didelphys/Unicornate	**37% – 40%**

Raga, Human Reproduction, 1997

Conclusions

- Uterine malformations are common, especially in the infertile woman.
- Most malformations are arcuate, with almost all others being septate.
- 3D ultrasound, because of its ease and accuracy, may be the gold standard for the diagnosis.

The future? It may be

3D sonohysterography

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NOTES

ULTRASOUND ASSESSMENT OF THE OVARY

Brad Van Voorhis, M.D.
Department of Obstetrics and Gynecology
University of Iowa College of Medicine
Iowa City, Iowa

LEARNING OBJECTIVES

At the conclusion of this presentation, participants should be able to:

1. Assess ultrasound as a diagnostic test for ovarian function.
2. Describe ovarian follicular development.
3. Discuss blood flow determination as a test of “follicular health.”

Ultrasound Assessment of the Ovary

Brad Van Voorhis, M.D.
Department of Obstetrics and Gynecology
The University of Iowa
Carver College of Medicine
Iowa City, Iowa

Learning Objectives

At the conclusion of this presentation, participants should be able to:

1. Assess ultrasound as a diagnostic test for ovarian function.
2. Describe ovarian follicular development.
3. Discuss blood flow determination as a test of "follicular health."

Disclosure:

Brad Van Voorhis M.D.

I was a co-investigator in a grant from ViaCell (study ended).

Outline and Objectives

- Ovarian ultrasound diagnostic tests
  - Ovarian reserve
- Ovarian follicular growth
  - Normal
  - Stimulated
- Ovarian follicular "health"
  - Blood flow

Aims of Ovarian Reserve Testing (ORT)

- Identify women at risk for poor response or no pregnancy.
- Identify women with a good prognosis.
- Data should inform us beyond age alone.
- Most ORTs better at predicting ovarian response than pregnancy (better at quantity than quality).

Broekmans et al. Hum Reprod Update 2006;12:685-718

Tests of Ovarian Reserve

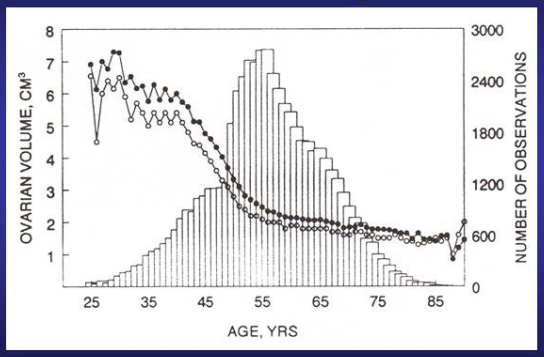
Indirect serum measures

- Cycle day 3 follicle-stimulating hormone (FSH) and estradiol (E_2) levels
- Inhibin B
- Müllerian inhibiting substance (anti-müllerian hormone [AMH])
- Stimulated FSH values

Ultrasound measures (direct observation)

- Ovarian volume
- Antral follicle counts

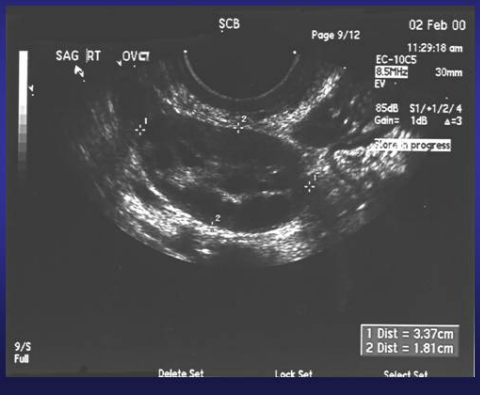
Mean Ovarian Volumes as Women Age



Pavlik et al. Gynecol Oncol 2000;77:410-12

Ultrasound Determination of Ovarian Volume

Formula: .52 x length (cm) x height (cm) x width (cm)



Ultrasound Infertility Ovarian Volume and IVF Outcome

Volume of the smallest ovary	Peak E_2 (pg/mL)	Eggs	Cancellation rate	Clinical pregnancy rate
< 3 cc	1524	11.6	22	28%
3-9 cc	1945	15.8	14	35%
> 9 cc	2907	21.3	0	46%

Syrop et al. Fertil Steril 1995;64:1167-71

Ovarian Volume Versus Day-3 FSH

- Independent of age, small ovarian volume predicted recovery of fewer oocytes and reduced pregnancy rate.
- Ovarian volume is superior to day-3 FSH as a measure of ovarian reserve.

Syrop et al. Hum Reprod 1999;14:1752-6

Large Ovarian Volumes Are Predictive of Ovarian Hyperstimulation Syndrome (OHSS)

"Pooled" ovarian volume	N	Risk of OHSS
< 10 cc	65	10%
> 10 cc	34	23.5%

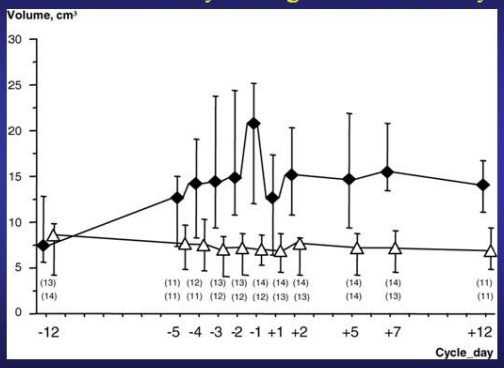
Danniger et al. Hum Reprod 1996;11:1597-9

Factors Affecting Ovarian Volumes

- Age (bigger decline after age 37)
- Current birth-control pill use
- Past cigarette smoking history
- Ovarian cysts (use smallest ovarian volume)

Syrop, Van Voorhis. Infert Reprod Med Clin N Am 2003;14:269-91

Changes in the Volume of the Dominant and Non-dominant Ovary During the Menstrual Cycle



Jokubkiene et al. Hum Reprod 2006;21:2661-8

Antral Follicle Counts (AFCs)

- Found to be superior to ovarian volumes
- Intra- and inter- observer differences in antral follicle counts and volumes are small among well-trained sonographers (worse at high numbers)
- Cycle-to-cycle variation is moderate

Syrop, Van Voorhis. Infert Reprod Med Clin N Am 2003;14:269-91

Transvaginal ultrasound reveals high normal ovarian volume (3.6 x 1.9 x 2.6 x π/6 = 9.3 cc) and multiple antral follicles

Antral Follicle Counts in Fertile Women

- Before age 37 years–counts decline by 4.8%/year.
- ≥ 37 years – counts decline by 11.7%/year.
- Decline is independent of the time in the cycle
- Decline is concordant with reduced primordial follicles histologically.

Scheffer et al. Fertil Steril 1999;72:845-51

Weaknesses of AFC Studies

- Variable definitions of "poor response"
- Failure to account for female age
- Different "cut-off" definitions
  - Follicle diameter 2-5 mm vs. 2-10 mm
  - Number ≤ 3 vs. ≤ 10
  - Variability in measurements

Hendricks et al. Fertil Steril 2005;83:291-301

AFC and Poor Response with IVF

(Studies > 100 cycles)

Author	AFC threshold	Sensitivity	Specificity	LR+	Proportion abnormal
Hsieh	24	.61	.94	10.0	9
Frattarelli	<4	.3	.96	7.4	6
Bancsi	<6	.81	.77	3.6	40
Frattarelli	<10	.87	.41	1.5	61

Ideal test
Sensitivity, specificity > .9
Likelihood ratio (LR) > 10 or < .1

Broekmans FJ et al. Human Reproduction Update, 2006.

AFC and Negative Pregnancy after IVF

(Studies > 100 cycles)

Author	AFC threshold	Sensitivity	Specificity	LR+	Proportion observed
Chang	<3	.13	.96	3.6	11
Bancsi	<4	.34	.88	2.9	27
Ng	<9	.60	.33	0.9	85
Fisch	<10	.24	.89	2.2	19

Ideal test
Sensitivity, specificity >0.9
LR + > 10 or < 0.1

Poor test
LR + 0.5-2.0

Broekmans F.J., et al Human Reproduction Update, 2006.

Antral Follicle Counts

- Test characteristics will vary depending on thresholds used.
- For poor response- AFC is considered clinically useful; use lower thresholds.
- For non-pregnancy – not a good test– need extremely low thresholds to be informative.

Broekmans et al. Hum Reprod 2006;12:685-718

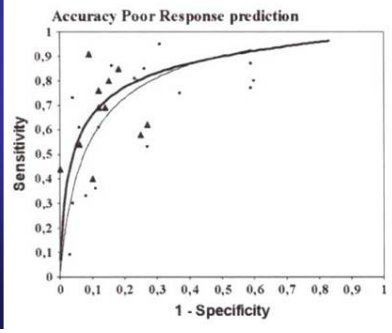
Meta-analysis of AFC vs. Basal Follicle-Stimulating Hormone (FSH)

- AFC performed better than FSH for predicting poor response.
- Neither test performed well for predicting pregnancy (AFC slightly better).

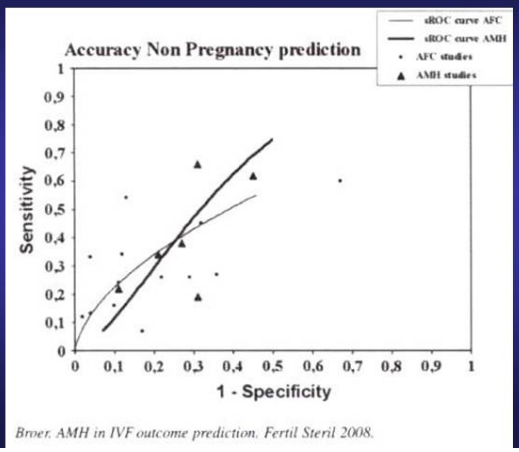
Hendricks et al. Fertil Steril 2005;83:291-301

Meta-analysis of AFC vs. Serum AMH

Accuracy of poor response and nonpregnancy predictions. AFC = antral follicle count; AMH = antimullerian hormone; ROC = receiver operating characteristic.



Meta-analysis of AFC vs. Serum AMH



Broer. AMH in IVF outcome prediction. Fertil Steril 2008.

Meta-analysis of AFC vs. Serum AMH

- Equal for predicting poor response
- AMH has advantage of lower variability and observer bias.
- Both are poor for prediction of pregnancy.

Broer et al. Fertil Steril 2009;91(3):705-14

Comparison of Tests of Ovarian Reserve

- Prospective study of 110 women
- Compared AFC, volumes, CCCT, FSH, AMH
- Best predictors of poor response: AMH, CCCT, FSH and AFC all similar
- Best predictor of hyper-response : AFC
- Best predictor of pregnancy: none

CCT= Clomiphene Citrate Challenge Test

Kwee J et al. Fertil Steril 2008

What do we do?

Use prior to IVF for counseling and selecting stimulation protocol

- Ovarian volume ≤3 cm (unsuppressed)
- Antral follicles 2-10 mm - ≤10 (combined)

Patients are not excluded on this basis do not wait for "optimal" AFC to start

Normal Unstimulated Ovarian Follicular Growth

- Dominant follicle emerges by day 8-12
- Growth is typically 1-2 mm/day
- Size of 20-24 mm with luteinizing hormone (LH) surge
- Growth curve may be slower in older women

Santoro et al. J Clin Endocrinol Metab 2003;88:5502-9

Stimulated Ovarian Follicular Growth

- Faster than natural rates
  - Averages about 2 mm growth/day mean diameter

With IVF – follicle size matters

- Egg retrieval rate optimal at 1-7 cc (12-24 mm)
- Implantation rates better at > 2 cc (>16 mm)
- Optimal pregnancy rates at 4 cc (20 mm)

Bergh et al. Hum Reprod 1998;13:1912-15

Cycle Disturbances in Older Women of Reproductive Age

- Ultrasound + hormonal measures daily
  - 26 older women (41-46 years)
  - 35 younger women (22-34 years)
- Older women had:
  - Shorter follicular phase
  - Shorter cycle length
  - Advanced follicle growth (starting in luteal phase)
  - Smaller follicular size before ovulation (19.8 mm vs. 21.5 mm)

Result: More "baseline ovarian cysts" in older women

van Zonneveld et al Hum Reprod 2003;18:495-501

Effect of Baseline Cysts on Stimulation Cycles

Difficult to study for these reasons:

- Must account for age of woman
- Simple versus complex cysts
- Hormonally active or not
- Stimulation type

Baseline Cysts and Stimulation Cycle Results

- Baseline cysts are a marker of poor ovarian reserve.
- Incidence is reduced by oral contraceptive pill (OCP) use.
- Effect on stimulation cycle + pregnancy rate – controversial!

My take:

- Hormonally inactive cysts unlikely to have an effect
- Complex cysts (CL cysts) unlikely to have an effect
- We cancel for hormonally active cysts, but data scarce

CL = corpus luteum

Segal et al. Fertil Steril 1999;71:274-7

Ultrasound Diagnosis of Endometriomas

- Ultrasound characteristics
  - Persistent, usually unilocular
  - Diffuse, low-level internal echoes
  - Hyperechoic foci in the wall
  - Absent central blood flow
  - "Kissing ovaries"

Endometrioma

Effect of Ovarian Endometrioma on IVF Outcome – a Meta-analysis of Observational Trials

# of eggs retrieved	-1.7 eggs (-3.1, -.2)
Pregnancy rate	1.17 (0.8, 1.6)
Clinical pregnancy rate	1.07 (0.6, 1.8)

No consensus on effects of surgical removal on subsequent IVF performance.

Gupta et al. RBM Online 2006;13(3):349-60

Blood Flow and Reproductive Function

- Reproductive system is an area of active angiogenesis:
  - Endometrium
  - Ovarian follicle
  - Corpus luteum
- Blood flow to the reproductive tract is high. Some have suggested reduced blood flow may adversely affect reproductive processes.

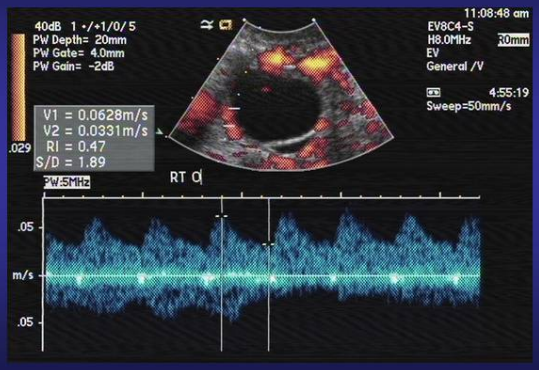
Doppler and Ovarian Follicular Vascularity

- Importance of ovarian vascularity is clear:
  - Increase in perifollicular blood flow at ovulation
  - Oxygen concentration of follicle has effects on egg quality and meiotic competence.
  - Follicular vascularity has been linked to embryo quality.

Campbell et al. Fertil Steril 1993;60:433-38

Conventional Doppler of Ovarian Follicle

Power Doppler of Follicular Blood Flow

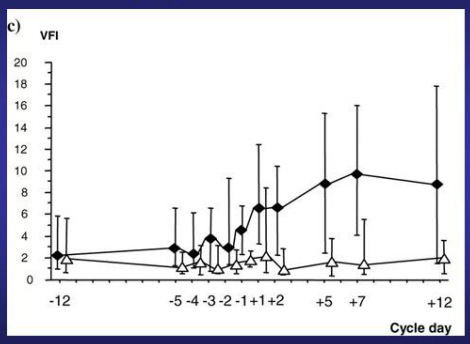


What Happens in the Ovary in the Natural Cycle?

- Study of 14 volunteers
  - Age 28 ± 5.2 years (24-44)
  - Multiple scans throughout 1 cycle
  - Ovarian, follicular volumes obtained
  - Total ovarian blood flow estimated by 3D power Doppler measures
- Vascular indices increased in dominant ovary late in follicular phase (1.7 fold) but even more in luteal phase (3.1 fold).

Jokubkiene et al. Hum Reprod 2006:21:2661-8

Changes in Vascularization Flow Index in the Ovary by 3D Flow Determination



Jokubkiene et al. Hum Reprod 2006:21:2661-8

Perifollicular Vascularity and IVF Outcome

Bahl et al. studied 200 cycles and 1,285 follicles prospectively – day of retrieval:

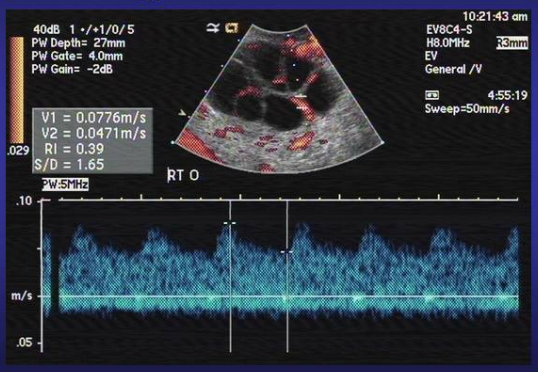
- No difference in uterine artery or intraovarian pulsatility index (PI) between pregnant and not pregnant cycles
- Eggs that came from highly vascularized follicles (>50% by power Doppler) were associated with higher pregnancy rates.

But

1. Most follicles (> 65%) well vascularized
2. Well-vascularized follicles were bigger.
3. Others have not confirmed this.

Bahl et al. Hum Reprod 1999;14(4):939-45
Polamba et al. Hum Reprod 2006;21(4):1055-61

Power Doppler of Follicular Blood Flow



Perifollicular Vascularity and IVF Outcome

- Further questions:
  - Is this finding independent of age and follicular size?
  - Is it superior to standard embryo selection techniques?
  - Can flow be modified?

Bottom Line

- Blood flow and infertility assessment and treatment:
  - Remain experimental at this time
  - Perifollicular flow is promising, but more work is needed.

Conclusions

- Ultrasound is valuable for ovarian reserve determination.
- Ultrasound also necessary for monitoring follicular development.
- Baseline cysts and ovarian endometriomas are associated with reduced ovarian reserve.

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NOTES

NOTES

ULTRASOUND FINDINGS IN POLYCYSTIC OVARY SYNDROME (PCOS): CURRENT CONTROVERSY

Brad Van Voorhis, M.D.
Department of Obstetrics and Gynecology
University of Iowa College of Medicine
Iowa City, Iowa

LEARNING OBJECTIVES

At the conclusion of this presentation, participants should be able to:

1. Explain the role of ultrasonography in the diagnosis of poycystic ovary syndrome (PCOS).
2. Describe ultrasound findings in PCOS.
3. Discuss the role of ultrasound in ovulation induction for PCOS.

Ultrasound Findings in Polycystic Ovary Syndrome (PCOS): Current Controversy

Brad Van Voorhis, M.D.
Director
In Vitro Fertilization Program
University of Iowa Carver College of Medicine
Iowa City, Iowa

Learning Objectives

At the conclusion of this presentation, participants should be able to:

1. Explain the role of ultrasonography in the diagnosis of polycystic ovary syndrome (PCOS).
2. Describe ultrasound findings in PCOS.
3. Discuss the role of ultrasound in ovulation induction for PCOS.

Disclosure:

Brad Van Voorhis, M.D.

I was a co-investigator on a study for ViaCell (study has since ended).

Polycystic Ovary Syndrome

- Prevalence 5%-10% of premenopausal women in the United States
- Clinical manifestations (*short term*): hirsutism, irregular menses, infertility
- Long-term associations: diabetes, hypertension, depression, ?coronary and cerebral atherosclerosis

Dokras. Sem Reprod Med 2008;26(1):39-44

Why Do Women with PCOS Have Multiple Follicles?

- Cause is unknown
  - Greater number of follicles
  - Greater entry into growing pool
  - Decreased apoptosis
  - Local effect of testosterone

Chang. Nature Clinical Practice. Endocrinology and Metabolism 2007;3(10:689-95
www.nature.com/clinpractice/endmet

1990 NICHD Guidelines

Patient demonstrates both:

- Clinical and/or biochemical signs of hyperandrogenism
- Oligo- or chronic anovulation

2003 Rotterdam Guidelines

Patient demonstrates 2 of 3 criteria:

- Oligo- or chronic anovulation
- Clinical and/or biochemical signs of hyperandrogenism
- Polycystic ovaries by ultrasound

2006 Androgen Excess Society (AES) Guidelines

Patient demonstrates both:

- Hirsutism and/or hyperandrogenemia
- Oligo-/anovulation and/or polycystic ovaries

For all guidelines, exclusion of other etiologies of androgen excess and anovulatory infertility is necessary.

Lujan et al. J Obstet Gynaecol Can 2008;30(8):671-9

Pitfalls in Diagnosing PCOS

Androgen Excess

Hyperandrogenemia
- Which androgens?
- Inaccurate normative ranges
- Imprecise analytic techniques

Hirsutism
- Subjective scoring system

Acne and alopecia
- Unconfirmed increase in prevalence and severity with PCOS

Lujan et al. J Obstet Gynaecol Can 2008;30(8):671-9

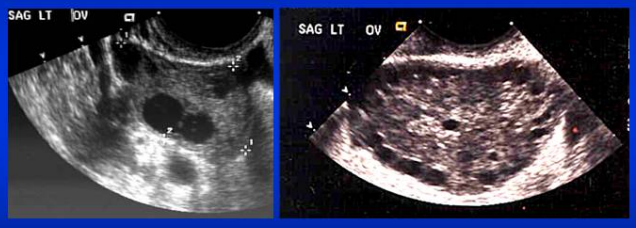
Pitfalls in Diagnosing PCOS

Anovulation
- Untimely progesterone measurement
- Assuming ovulation with regular menses

Polycystic ovaries
- Use of multiple criteria
- Subjective nature of some measures
- Lack of specificity for some criteria

Lujan et al. J Obstet Gynaecol Can 2008;30(8):671-9

Ultrasound Evaluation of PCOS Ovaries



Ultrasound Criteria for PCOS

ESHRE/ASRM Consensus Groups

12 or more follicles measuring 2-9 mm

and/or

Ovarian volume of 10 cm^3

(length X width X thickness X 0.05)

- One ovary meeting these criteria is sufficient.
- Repeat scan if cyst > 10 mm in diameter is present.
- Not to be used if woman is on birth control pills (BCPs)

ESHRE = European Society of Human Reproduction and Endocrinology

Brown and Chang. US Quarterly 2007;23:233-8

Blanchette-Porter M. Semin Reprod Med. 2008;26(3):241-51

Ultrasound Criteria for PCOS

214 PCOS women

112 women with "normal" ovaries

Excluded PCO ovaries in control group!!

FNPO	Area under the ROC curve	Threshold	Sensitivity (%)	Specificity (%)
2-9 mm	0.937	10	86	90
		12	75	99
		15	58	100

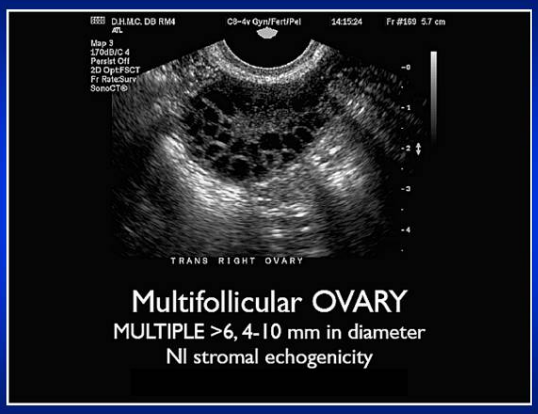
FNPO = follicle number per ovary
ROC = receiver operating characteristic

Jonard et al. Hum Reprod 2005;20(10):2893-8

Problems with Ultrasound Criteria

- Criteria of 12 follicles has been questioned
  - Allemand suggested 18 as more appropriate (20 for 3-D scan)
- Problem is specificity – many women without PCOS have 12 or more follicles/ovary
  - Multifollicular ovaries
    - Young women in early follicular phase
    - Puberty
    - Weight-loss-related amenorrhea

Brown and Chang. US Quarterly 2007;23:233-8



Multifollicular OVARY
MULTIPLE >6, 4-10 mm in diameter
Nl stromal echogenicity

Blanchette-Porter M. Semin Reprod Med. 2008;26(3):241-51

Prevalence of Ultrasound (US) Findings of Polycystic Ovaries

	Prevalence n (%)
Normal controls	257 (23)
Amenorrhea	73 (26)
Oligomenorrhea	75 (87)
Hirsutism	25 (92)

Mishell, Daniel Atlas of Clinical Gynecology

Other Ultrasound Criteria for PCOS

- Increased stromal echogenicity?
  - Subjective
  - Not confirmed in objective studies using 3-D scans
- Ovarian vascularity by Doppler
  - No consistently demonstrated differences
- Increased stromal volume (7 cm^3) or area (5 cm^2) reported by some for PCOS

Brown and Chang. US Quarterly 2007;23:233-8

Fulghesu et al. Hum Reproduction 2007;22:2501-5

Stromal/Area (S/A) Ratio

- Maximal plane section ovary
- Ovarian stromal area, outlining with the caliper the peripheral profile of the central hyperechoic area
- Caliper outlines the external limits of ovary
- Calculated by adding the sizes of each ovary then dividing by 2
- Criteria of Adams = threshold 0.34 (0.32)
  - 10 or more follicles 2-8 mm
  - Echo-dense central stroma

Belosi C et al. Human Reprod 2006;21(12);3108-15

Ultrasound Criteria for PCOS

- Increased stromal area compared to total ovarian area may be a marker of PCOS.
- S/A > 0.32 was significantly associated with elevated androgen levels in a study of 418 women with PCOS.

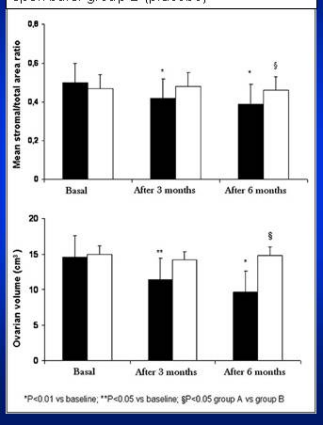
Fulghesu et al. Hum Reproduction 2007;22:2501-5

Therapy Can Affect PCOS Ultrasound Findings

- Italian study of 28 normal-weight women with PCOS
- 28 randomized to metformin 500 mg twice a day vs. placebo

Romualdi et al. Fertil Steril 2009. In press.

Stromal/total area ratio and ovarian volume modifications in PCOS patients after 3 and 6 months. *Solid bars:* group A (Metformin); *open bars:* group B (placebo)

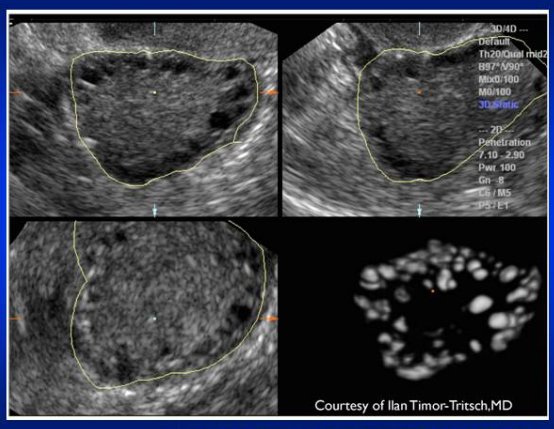


*P<0.01 vs baseline; **P<0.05 vs baseline; §P<0.05 group A vs group B

3-D US in PCOS

- Better definition of follicular count
- More accurate volumetric measurements
- Stromal volume = total ovarian volume - total follicular volume
- Quantitative assessment of stromal echogenicity and vascular flow
- Should PCO definition be reevaluated?

Blanchette-Porter M. Semin Reprod Med. 2008;26(3):241-51



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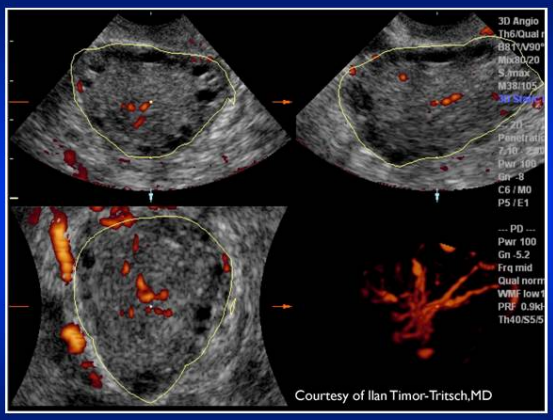


Blanchette-Porter M. Semin Reprod Med. 2008;26(3):241-51

Blanchette-Porter M. Semin Reprod Med. 2008;26(3):241-51

Ovarian Imaging by Magnetic Resonance Imaging (MRI) in PCOS Patients

- May have advantages in obese or virginal patients
- Criteria not yet established
- Cost prohibitive at this time

Brown and Chang. US Quarterly 2007;23:233-8

Brown and Chang. US Quarterly 2007;23:233-8

Ultrasound Findings of PCOS Persist into Middle Age

Swedish study of women diagnosed with PCOS between 1987-1995

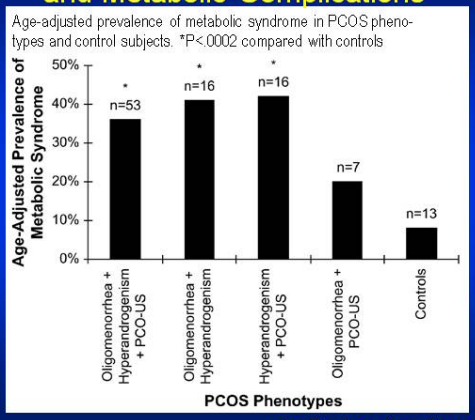
	Findings	
	PCOS (n=52)	Controls (n=56)
Age	42.4 ± 4.5	41.5 ± 4.6
Ovarian volume	9.5 ± 0.9	6.6 ± 0.5
Antral follicles	11.7 ± 1.7*	5.0 ± 0.3
FAI	5.1 ± 0.8*	2.0 ± 0.2
AMH	39.9 ± 6.1*	15.7 ± 2.1

- Equal lifetime fecundity
- Better ovarian reserve?
- *p < 0.05

FAI = free androgen index
AMH = anti-müllerian hormone

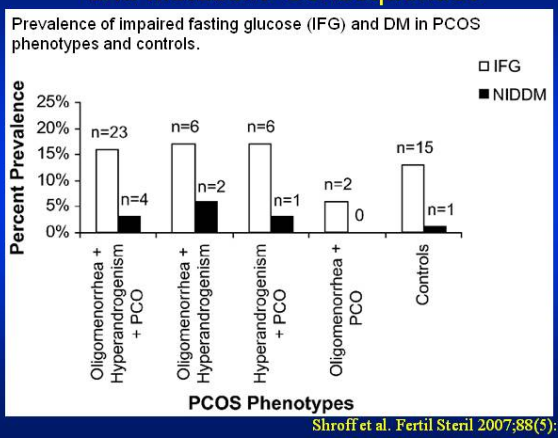
Hudecova et al. Hum Reprod 2009;1(1):1-8

PCOS: Ultrasound-based Diagnosis and Metabolic Complications



Shroff et al. Fertil Steril 2007;88(5):1389-95

PCOS: Ultrasound-based Diagnosis and Metabolic Consequences



Shroff et al. Fertil Steril 2007;88(5):1389-95

Endometrial Echo Thickness in PCOS

- Endometrial hyperplasia increased
  - Increased risk of focal atypia
- Anovulation prolonged stimulatory and mitogenic effects of unopposed estrogen
- Trophic effects hyperinsulinemia

Blanchette-Porter M. Semin Reprod Med. 2008;26(3):241-51

Blanchette-Porter M. Semin Reprod Med. 2008;26(3):241-51

Use of Ultrasound for Clomiphene Citrate (CC) – Intrauterine Insemination (IUI) Cycles (Ovulatory Women)

	US – hCG	Urine LH surge
Randomized	75	75
Completed (1 cycle)	71	58
Pregnancy rate (3 cycles)	31%	25%

No difference in pregnancy rate

Higher drop-out rate in LH surge group (31% vs. 11%)

Bottom line: no evidence for improved pregnancy rate with routine ultrasound

hCG = human chorionic gonadotropin
LH = luteinizing hormone

Queenan et al. Fertil Steril 2006;85:401-6

Is Ultrasound Helpful in Clomiphene Citrate/IUI Treatment?

Meta-analysis results
(retrospective studies and cross-over studies)

	CC - ultrasound - hCG - IUI	CC - LH surge - IUI
All patients	9.5%	11.7%*
Ovulatory dysfunction	16.1%	8.1%
Male factor	9.7%	12.2%
Unexplained	7.2%	8.4%

* Odds ratio (OR) 0.74; 95% confidence interval (CI) 0.57 – 0.96

Other comparisons showed no difference

Kosmos et al. Fertil Steril 2007;87:607-12

Use of Ultrasound for Clomiphene Citrate Cycles - My Opinion

- Difficulty in detecting LH surge
- Patient frustration
- After 4-6 ovulatory cycles but no pregnancy- evaluate mid-cycle endometrium

Ovulation Induction with Clomiphene Citrate

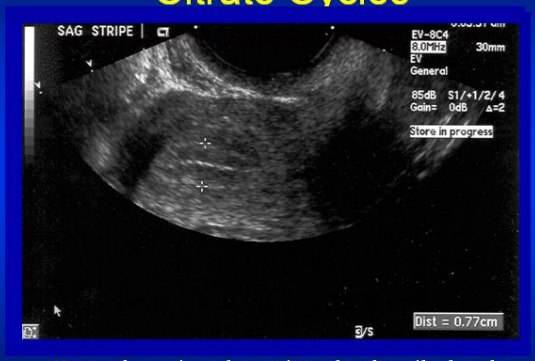
Ovulation rate – 60%-85%

Pregnancy rate – 10%-20%/cycle

- Discrepancy may be explained by anti-estrogen effect on reproductive tract.

Fisher et al. Fertil Steril 2002;78:280-285

Endometrium in Clomiphene Citrate Cycles



Hypoechogenic endometrium also described as the triple-line or ring pattern

Endometrium in Clomiphene Citrate Cycles

Hyperechogenic, thin endometrial pattern

Abnormal Endometrium on Clomiphene Citrate

- Controversial
- Stripe < 6 mm
  - CC cycles – 9%
  - CC+hMG – 11%
  - hMG alone – 2%
- 0 pregnancies in 43 cycles

Dickey et al. Fertil Steril 1993;59:756-90

hMG = human menopausal gonadotropin

Effect of Stripe Thickness on Pregnancy Rates with Clomiphene Citrate

- 15%-50% will have "thin" stripe
- Few to no pregnancies if stripe ≤ 6 mm
- Non-trilaminar pattern also associated with poor prognosis
- Can be reversed with exogenous estrogen

Fisher et al. Fertil Steril 2002;78:280-285

Trial of Letrozole in Women Who Failed CC Treatment

(No ovulation or ovulation with stripe ≤ .5 cm.)

	Letrozole	CC
N	12	12
Stripe thickness	0.8 cm*	0.6 cm.
Follicles	2	2
E_2 (pg/mL)	320*	546
Ovulatory rate	75%	
Pregnancies	2	

Mitwally and Casper. Fertil Steril 2001;75:305-9

Conclusions

- PCOS ultrasound criteria are not perfect—poor specificity.
- PCOS in the absence of elevated androgens may have different metabolic consequences.
- Monitoring of folliculogenesis in PCOS is not routinely needed, but can be helpful in some circumstances.

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NOTES

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EARLY PREGNANCY FAILURES FOLLOWING IN VITRO FERILIZATION

Josef Blankstein, M.D., A.R.D.M.S.
Professor and Chairman
Department of Obstetrics and Gynecology
Rosalind Franklin University
The Chicago Medical School
Chicago, Illinois

LEARNING OBJECTIVES
At the conclusion of this presentation, participants should be able to:

1. Describe the physiology of early pregnancy.
2. Explain the various etiologies of early pregnancy failures.
3. Discuss the importance and ways of assessing multiple pregnancies.

Early Pregnancy Failures Following In Vitro Fertilization

Josef Blankstein, M.D., A.R.D.M.S.
Professor and Chairman
Department of Obstetrics and Gynecology
Rosalind Franklin University,
The Chicago Medical School
Chicago, Illinois

Learning Objectives

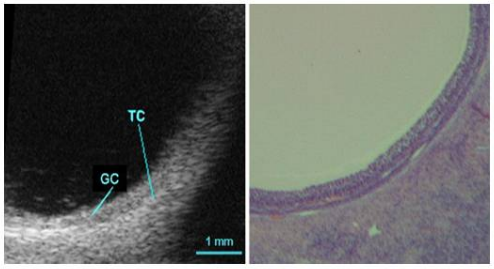
- Describe the physiology of early pregnancy.
- Explain the various etiologies of early pregnancy failures.
- Discuss the importance and ways of assessing multiple pregnancies.

Disclosure

Josef Blankstein, M.D.
Nothing to disclose

Antrum, Granulosa Cells (GCs) and Theca Cells (TCs) in a Preovulatory Follicle

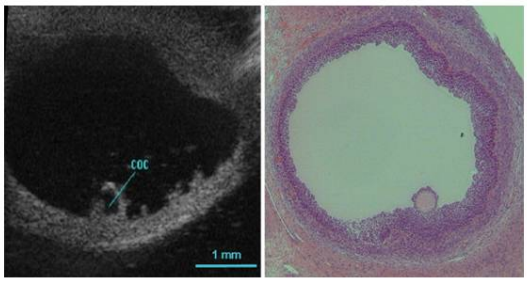
Ultrasound biomicroscopy Histology



Pallares et al. Fertil Steril 91;622,-2009

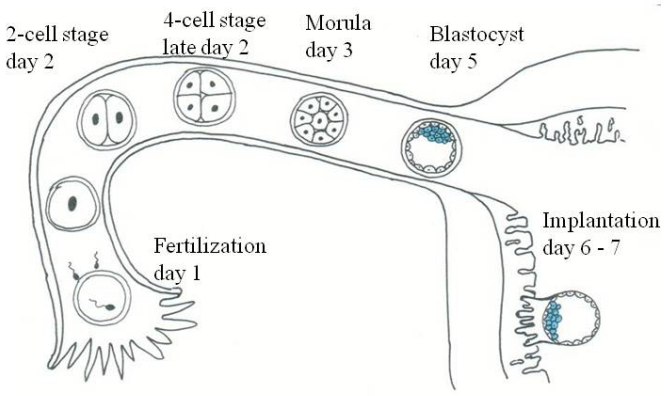
Cumulus-Oocyte Complex (COC)

Ultrasound biomicroscopy Histology



Pallares et al. Fertil Steril 91;622,-2009

Week 1:



Blastocyst Implantation

- 1-1.5 weeks following fertilization
- ↑ blood flow to the uterus
- Thickening of the endometrium- decidual reaction
- Not a definite ultrasonographic sign

Patient Expectations

- Provide women with early status of their pregnancies
- Earlier confirmation of normal pregnancies
- Earlier identification of pregnancy failures

AIUM Ultrasound Recommendation in the First Trimester of Pregnancy

- Confirm the presence of an intrauterine pregnancy (IUP)
- Rule out ectopic pregnancy
- Date the pregnancy
- Diagnose multiple gestations
- Confirm cardiac cavity
- Evaluate maternal pelvic masses and/or uterine abnormalities
- Evaluate a suspected hydatidiform mole

Blanchette Porter M; J.Ultrasound Med., 2009 28; 125-138

AIUM = American Institute of Ultrasound in Medicine

IUP and Cervix

Do Not Scan in a Vacuum

- Know clinical history
- Human chorionic gonadotropin (hCG) levels allow you to have expectation of sonographic findings.
- Assess pregnancy viability
  → A 50% increase in hCG every 2 days generally indicates a normal pregnancy.

The Contributions of hCG Measurements

- When using transvaginal technique, the hCG discriminating level in detecting an IUP has been shown to be 1000-2000 mIu/mL
- Trophoblastic disease: declining hCG levels are consistent with effective treatment.

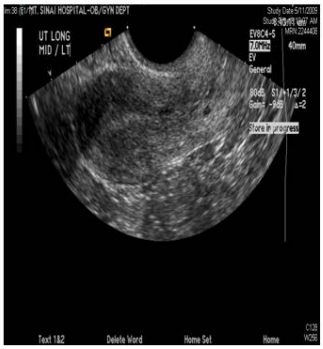
Clinical Dilemma

Patient referred from infertility clinic at 5 ½ weeks with:

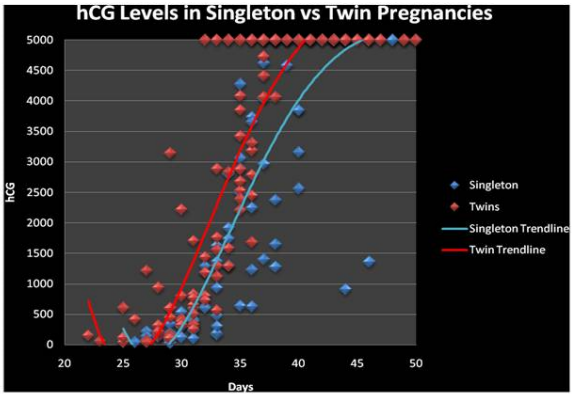
- **Mild abdominal pain**
- **hCG of 4000 mIu/mL**
- **Ultrasound: empty uterus**

You recommend:

- **Laparoscopy**
- **Methotrexate**
- **Dilation and curettage (D&C)**
- **Repeat testing in two days**

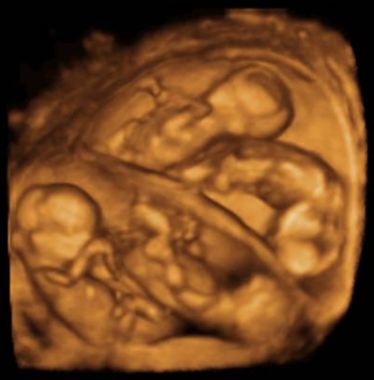


Nadya Suleman, 33 years old, Octomom.
hCG 4000 ▸ Ultrasound "empty uterus"



Chicago IVF- unpublished data

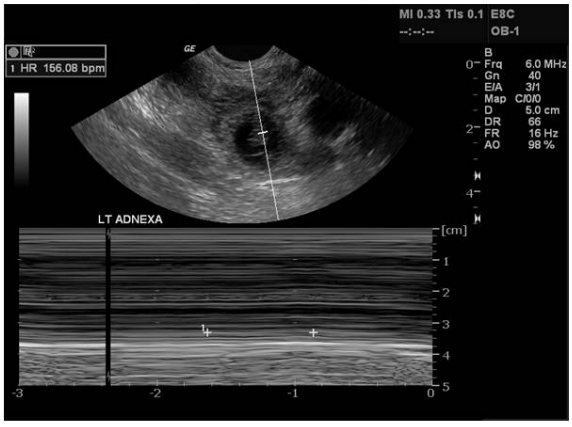
Quadruplets



Ectopic Pregnancies

- The absence of IUP in conjunction with beta hCG above the discriminatory threshold suggests ectopic pregnancy.
- The confirmatory finding is an extra-uterine gestational sac.
- Suggestive findings include an empty uterus.

Live Ectopic



Ectopic Pregnancy Risk with Assisted Reproductive Technology Procedures

- Out of 94,118 ART pregnancies, 2.1% were ectopic.
- For zygote, intrafallopian transfer was 3.6%
- With use of donor oocytes, 1.4%
- With gestational surrogate carrying the pregnancy, 0.9%

Conclusion: Ectopic risk varied according to ART procedure (level of evidence: II-2)

Heather B. Clayton et al. Obstetrics and Gynecology, 2006

Retrospective Study of Confirmed Ectopic Pregnancies

- The sample group comprised 66 patients with confirmed ectopic pregnancies.
- The comparison group consisted of 60 randomly selected pregnant patients that had normal pregnancies during this period.

Mt. Sinai, Chicago – Dogan et al., unpublished data

Results

	Ectopic pregnancy (N=66)	Normal pregnancy (N=60)
Adnexal mass	92.4%	1.7%
Free fluid	82%	20.0%

Mount Sinai Hospital, Chicago, IL

Ultrasonographic markers, such as presence of an adnexal mass and free fluid in the cul-de-sac, are significant markers that raise suspicion of an ectopic pregnancy.

Early Pregnancy Failure

- Major criteria
  - No viable gestational sac (GS) with serum hCG above discriminatory level of 1500-2000 mIU/mL
  - No visible yolk sac (YS) when gestational sac measures > 10 mm
  - No viable fetal pole when mean sac diameter (MSD) measures 16-18 mm or more
  - No viable fetal heart activity when embryo measures 5 mm or more

Paspulati RM, et al; Radiol Clin N Am 42:297-314 2004

Sonographic Features of a Normal Gestational Sac

- Shape: Round or oval
- Position: Fundal or middle portion of uterus
- Contour: Smooth
- Wall (trophoblastic reaction): Echogenic; 3 mm or more in thickness
- Internal landmarks: Yolk sac present when gestational sac is larger than 10 mm; embryo present when gestational sac is larger than 18 mm
- Growth: 1 mm/day (range: 0.7 mm to 1.5 mm/day)

Nyberg et al.

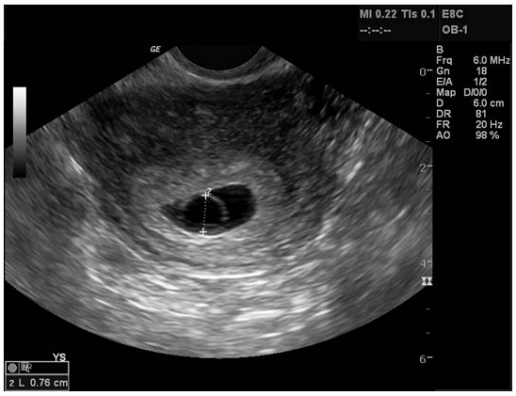
Case 3 – Normal Early Pregnancy

Yolk Sac

- First structure visualized within gestational sac
- Primary source of nutrition exchange between mother and embryo
- Very round, bright rim
- ≤ 6 mm
- Confirm an IUP; 100% positive predictive value (PPV)

Case 3 – Early Intrauterine Pregnancy with a YS

Case 1 - Enlarged Yolk Sac: Bad Prognostic Sign



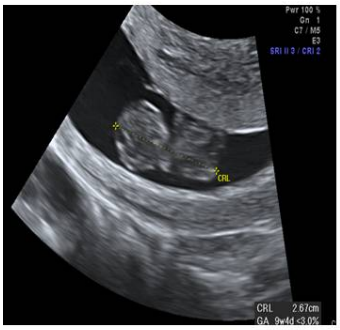
Embryo

- The embryo should be visualized by transvaginal ultrasound (TVUS) when the gestational sac measures greater than 18 mm.
- Embryonic cardiac activity should always be seen when an embryo measures greater than 5mm.
- If the length of the embryo is less than 5mm, follow-up ultrasound (US) should be performed.

Paspulati RM, et al; Radiol Clin N Am 42:297-314 2004

Crown-Rump Length (CRL)

- The CRL is the most accurate of all measurements.
- The correct measurement is obtained from the top of the head to the bottom of the rump (excluding the legs).
- Embryonic growth is at the rate of 1 mm per day.



Cardiac Activity

- 41% of embryos 3 mm or less without discernable cardiac activity ultimately proved normal.
- All cardiac activity when ultimately present was seen by 4 mm embryonic size.

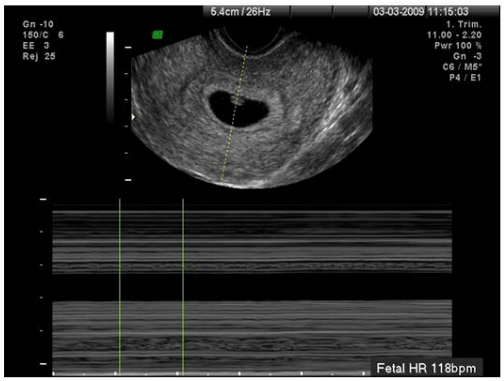
Goldstein, S.R. Obstet Gynecol 1992;80;670-2

Embryonic Cardiac Activity

- Absence of cardiac activity in embryos of 4 mm or more most likely means:
  - Early embryonic death
- The lack of cardiac activity in embryos of 3 mm or less is non-diagnostic:
  - Re-scan in 3-5 days

Goldstein, S.R. Obstet Gynecol 1992;80;670-2

Early Live Pregnancy

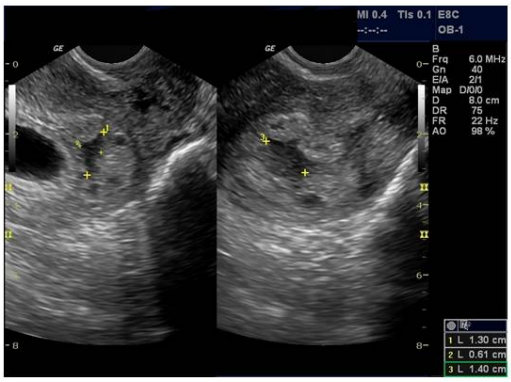


Pregnancy Outcome after Sonogram Demonstrates Fetal/Embryonic Cardiac Activity

- Prospective study
- N=556 cases
- Overall pregnancy loss after positive cardiac motion was 8.8%.
- Additional abnormalities, such as subchorionic hematoma (SCH), increase the loss to 15.2%.
- A symptomatic patient can be reassured after a normal scan that her prognosis is similar to that of an asymptomatic patient with a normal sonogram.

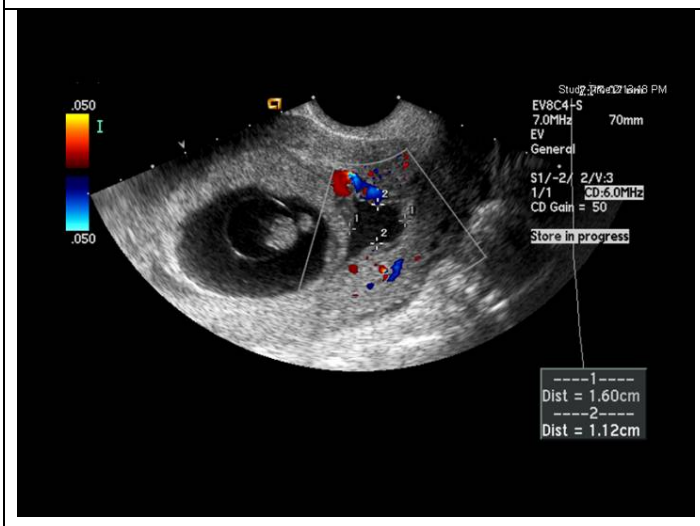
Frates et al. J Ultrasound Med 1993; 12; 383-386

Case 12 - Small SCH



Case 8 – Small SCH

Case 11 - Moderate SCH



Sonographic Features of Fetal First Trimester Heart Rates (HRs)

Gestational age (weeks)	Mean fetal HR (~beats/minute)
5	92-109
6	112-136
7	112-140
8	126-160
9	126-150
10	126-150
11	120-150
12	125-160

Hagen-Ansert S; text book of Diagnostic Ultrasonography sixth edition; Mosby P 994; 2006

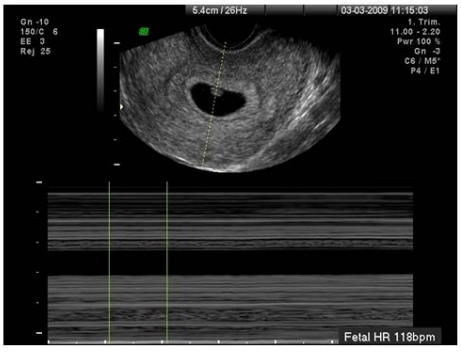
Early Pregnancy Failure

- Slow embryonic heart rate
- Survival:
  - 92% if heart rate is normal
    - GA 6.2 weeks or less, 100 bpm or more
    - GA 6.3-7 weeks, 120 bpm or more
  - 0% if heart rate < 85 bpm and GA 6-8 weeks

Doubilet PM J Ultrasound Med 1999;18;537-41

GA = gestational age
bpm = beats per minute

Early Live Pregnancy



Fetal/Embryonic Heart Activity

- What does the presence of normal fetal (>10 weeks) or embryonic (<10 wks.) heart activity mean?
  - 90-96% of patients presenting with bleeding between 7 and 11 weeks will continue the pregnancy.[1]
  - In women with recurrent miscarriage, the loss rate = 17%. [2]
  - Age matters [3]
    - < 36 years 4.5% loss
    - 36-39 years 10% loss
    - 40 + years 29% loss

1 Wilson RD, Obstet Gynecol
2 Van Leewen, Am J Obstet Gynecol 1997

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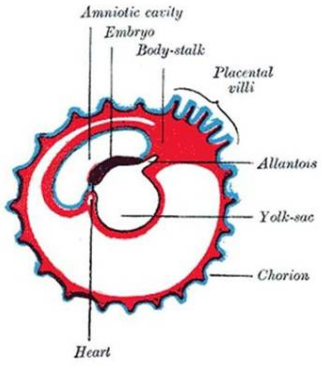
Case 4 – Early Live Pregnancy



Points To Remember

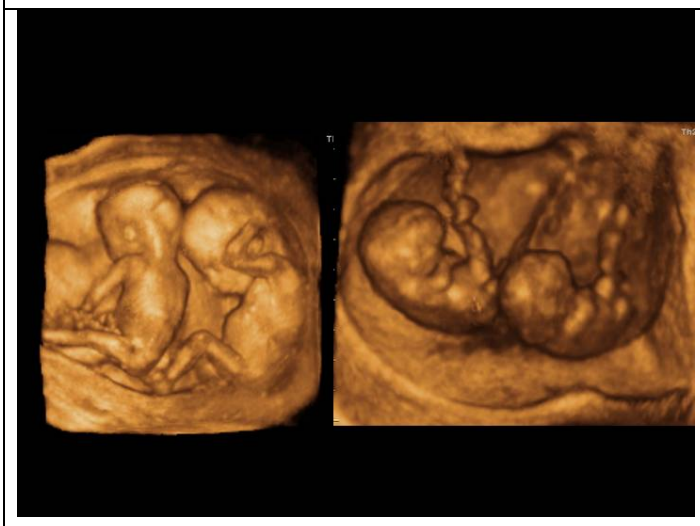
	Gestation of earliest ultrasound appearance	
	Transvaginal scan	Transabdominal scan
Intrauterine sac (2-4 mm)	4.5 weeks	5.5 weeks
Fetal heart (FH) pulsation, CRL 2-4 mm	5 weeks	6 weeks
Yolk sac (10 mm)	5 weeks	6 weeks

Smith N, Smith AP: Obstetric and Gynecological ultrasound: Churchill Livingstone 25.2006

AIUM Ultrasound Recommendations in the First Trimester of Pregnancy

- Embryonic number should be reported
  - Amnionicity and chorionicity should be documented for all multiple pregnancies when possible.

Blanchette Porter M, et al. J.Ultrasound Med, 2009 28; 125-138



Multiple Gestations

- High-risk pregnancy: significant morbidity and mortality compared to singleton pregnancies
- In ART pregnancies:
  - In 2000, 35% of all births in the United States were multiples.
  - This rate is 10 times higher than the 3% multiple infants in the general population.

Speroff L; Fritz M: Clinical Gynecologic Endocrinology and Infertility, 7th Edition, 2005 P 1249; Lippincott, Williams & Wilkins

Clinical Complications Associated with Twin Pregnancy

- **Maternal complications**
  - Anemia
  - Preeclampsia/ eclampsia
  - Pre-/post-partum hemorrhage
- **Fetal complications**
  - Premature delivery
  - Difficult delivery
  - Prolapse of an umbilical cord
  - Hypoxia of second twin due to premature separation of the placenta
  - Growth restriction due to placental insufficiency

Complications of Monochorionic Twin Gestations

- **Twin-twin transfusion syndrome (TTTS)**
  - Due to the shared placenta (artery-to-vein anastomoses shunt blood away from the donor twin)
- **Sonographic findings**:
  - Donor twin:
    - Small for dates
    - Oligohydramnios
    - "Stuck" twin with empty bladder and restricted movement
  - Recipient twin:
    - Hydropic
    - Ascites
    - Enlarged liver, heart and kidneys
    - Polyhydramnios

Complications of Monochorionic Twin Gestations

- **Twin embolization syndrome**
  - The passage of thromboplastic material from a dead monochorionic twin to the live twin
- **Sonographic findings:**
  - Intrauterine death of co-twin
  - Hydrops
  - Polyhydramnios

Multiple Gestations

- Monochorionic-diamniotic twins appear to be contained within one chorionic sac; two amnios, two yolk sacs and two embryos are identified.

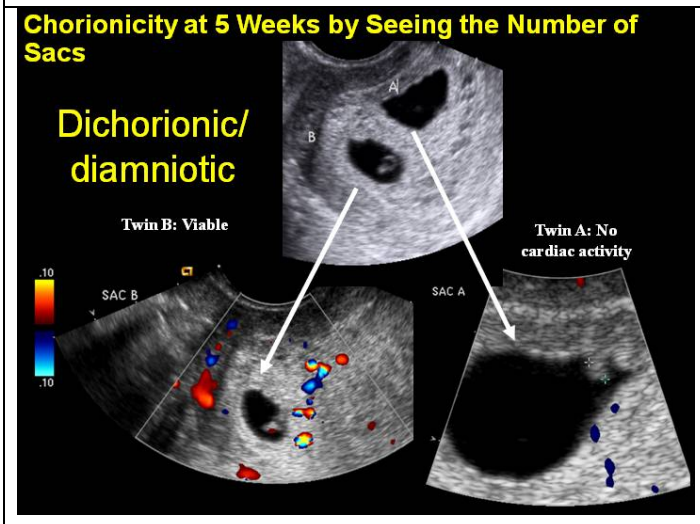
Rule out monozygotic, Monoamniotic-monochorionic.

- The two cord insertions into the placenta are in close proximity.
- Color Doppler may demonstrate cord entanglement.
- Occurs in 1% of all monochorionic twins
- 50% mortality rate

Case 9 – 6 Week Monochorionic/Diamniotic

Amnioncity at 8 Weeks: Amnion Is Seen Separately from the Embyro (Monochorionic/Diamniotic)

Chorionicity at 5 Weeks by Seeing the Number of Sacs



In Dichorionic, Diamniotic Twins, the Dividing Membranes Appear Thicker (Regress in the 2nd and 3rd Trimesters)

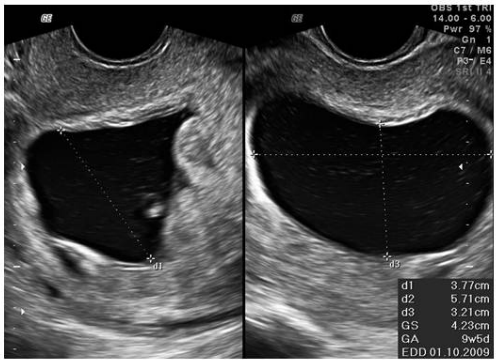
	Sonographic Determination of Chorionicity and Amnionicity in First Trimester Twin Gestations			
Distribution	Gestational sacs	Yolk sacs	Embryos/ sac	Amniotic cavities
DC, DA	2	2	1	2
MC, DA	1	2	2	2
MC, MA	1	1 or partially divided	2	1

DC = dichorionic; DA = diamniotic; MC = monochorionic; MA = monoamniotic

Threatened Miscarriage

- Diagnosis
  - Not able to diagnose sonographically
- However, these patients are at slightly higher risk of obstetric complications and premature deliveries.

Anembryonic Gestation



Anembryonic Pregnancy

- Developmental arrest before formation of the embryo
- Failure to reveal yolk sac or embryo
- Look for double decidual sac, which will confirm an IUP, and not pseudo-gestational sac.

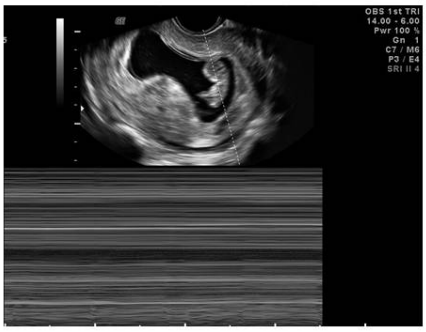
Laing F; 2008

Missed Miscarriage

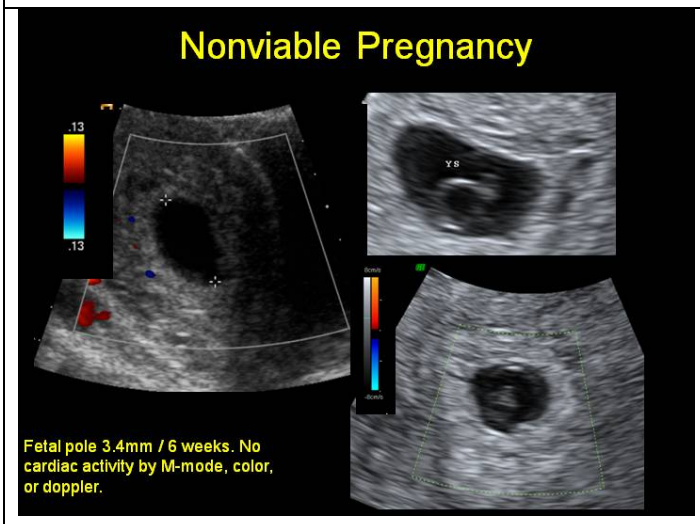
- The presence of an embryo (≥5 mm) within the uterus, without evidence of cardiac activity.
  - Sonographic findings
    - Presence of a gestational sac with or without a fetal component
    - Absence of fetal cardiac activity
    - Acoustic shadowing indicating the presence of calcified fetal parts
    - Embryo size and uterus less than expected for dates

Paspulati RM, et al. Radiol Clin N Am 42:297-314 2004

7 Weeks' Gestation – No Fetal Heart Beat (FHB)



Nonviable Pregnancy



Fetal pole 3.4mm / 6 weeks. No cardiac activity by M-mode, color, or doppler.

Case 2 - Early Fetal Pole (FP) – No FHB on Doppler

Fetal pole 11mm

Typical Sonographic Findings of Threatened Miscarriage and Abnormal Pregnancy

Term	Ultrasound findings
Threatened miscarriage	-Embryo with cardiac activity -Empty gestational sac (5-6.5 weeks) that subsequently develops with embryo -Empty uterus (3-5 weeks)
Complete miscarriage	Empty uterus
Incomplete miscarriage	Typical thickened and irregular endometrium or fluid within endometrial cavity
Miscarriage in progress	Gestational sac in the process of expulsion

Nyberg DA, et al. Transvaginal Ultrasound. St Louis, Mosby-Year book, 1992

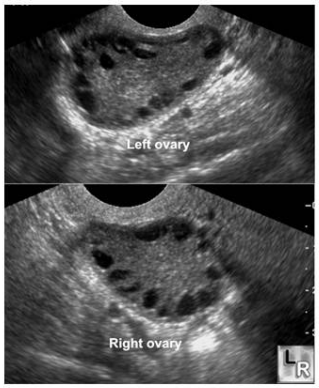
Case 10 – 6 Days Post-Dilation and Curettage (D&C) Beta-hCG >1000

Conventional IVF: Concerns

- High success rates achieved at the expense of ovarian hyperstimulation syndrome (OHSS) and MULTIPLE pregnancies
- Medication side effects
- Cost of medication

In Vitro Maturation (IVM)

Immature oocyte retrieval and subsequent oocyte maturation in vitro (IVM) is a new development in assisted reproductive technology (ART).



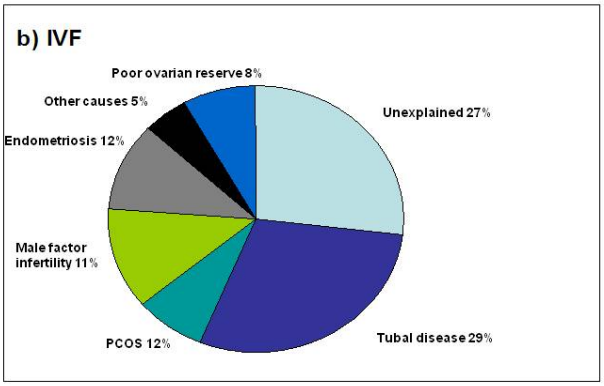
IVM

- Selection of patients
  - Polycystic ovary syndrome (PCOS)
  - Regular cycling women
- Criteria for success
  - PCOS
  - High antral follicle count
  - Young age

Pregnancy Loss in Pregnancies Conceived after in Vitro Oocyte Maturation, Conventional in Vitro Fertilization, and Intracytoplasmic Sperm Injection (ICSI)

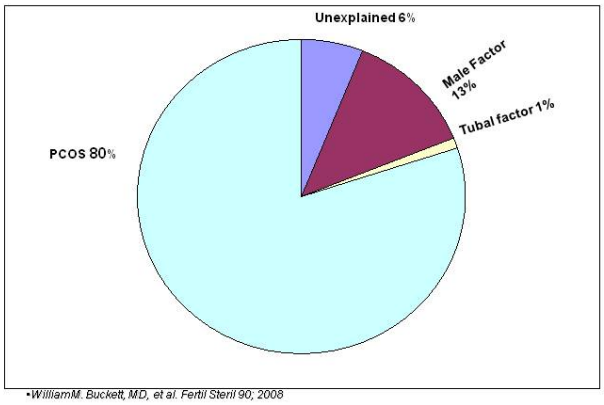
- *William M. Buckett, MD, et al. Fertil Steril 90; 2008*

Primary Causes of Infertility in Pregnancies Conceived after IVF



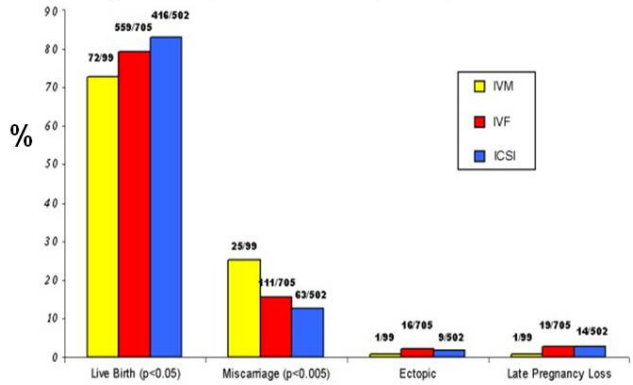
•WilliamM. Buckett, MD, et al. Fertil Steril 90; 2008

Primary Causes of Infertility in Pregnancies Conceived after IVM



•WilliamM. Buckett, MD, et al. Fertil Steril 90; 2008

Pregnancy Outcomes per Clinical Pregnancy after IVM, IVF, and ICSI



•WilliamM. Buckett, MD, et al. Fertil Steril 90; 2008

Miscarriage after:

- IVM 25%
- IVF 16%
- ICSI 13%

- Possible explanation: predisposition in women going through IVM
- Treatment-mediated effect
- Patient with PCOS have higher miscarriage rate regardless of whether they conceived after IVM or IVF:
  - ↑ **related to PCOS**

•*WilliamM. Buckett, MD, et al. Fertil Steril 90; 2008*

Miscarriage after Fertility Treatment: "The Good News…"

After accounting for "biochemical pregnancies" –

The overall spontaneous miscarriage rate is similar to that expected for the general population.

Balen; 2003

Thank you

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NOTES

Course #10 Test Questions

1. The following anovulatory patients were induced with gonadotropins. Human chorionic gonadotropin (hCG) was administered when estradiol levels were 2,200 pg/mL. In which one of these scenarios is the patient more prone to develop hyperstimulation?

    a. Ultrasound on the day of hCG revealed 12 follicles measuring between 18 and 22 mm.
    b. Ultrasound on the day of hCG revealed 16 follicles measuring between 18 and 22 mm
    c. Ultrasound on the day of hCG revealed 12 follicles measuring less than 10 mm.
    d. Ultrasound on the day of hCG revealed 16 follicles measuring less than 10 mm.
    e. Ultrasound on the day of hCG revealed 22 follicles measuring 8 to 9 mm.

2. A patient is referred from an infertility clinic at 5 weeks' gestation with mild abdominal pain, hCG of 4000, and ultrasound showing "empty uterus." What is your recommendation?

    a. Laparoscopy
    b. Dilation and curettage (D & C)
    c. Methotrexate
    d. Repeat hCG and ultrasound in two days
    e. Repeat hCG and ultrasound in one week

3. A 37-year-old female has been told she has the most common type of uterine malformation, meaning that her uterus is:

    a. Bicornuate
    b. Unicornuate
    c. Septate
    d. Arcuate
    e. Tricornuate

4. When scanning women during the infertility evaluation, several abnormalities can be found that may affect assisted reproductive treatment outcomes. Which one of the following statements is true?

    a. Intracavitary fibroids have no effect on IVF outcomes.
    b. Hydrosalpinges are associated with reduced pregnancy rates after IVF.
    c. The endometrial thickness has no effect on the pregnancy rate with IVF.
    d. The presence of endometrial fluid due to a hydrosalpinx has no effect on IVF outcome.
    e. There is no evidence that removal of polyps leads to higher pregnancy rate with gonadotropin – intrauterine insemination (IUI) cycles.

(continued)

5. A 21-year-old woman with irregular menstrual cycles presents to your office wondering if she has polycystic ovary syndrome (PCOS). Which one of the following findings is consistent with a diagnosis of PCOS?

    a. 5 follicles between 2 and 9 mm in size in her right ovary and 5 follicles between 2 and 9 mm in size in her left ovary.
    b. An ovarian volume of 11 mL
    c. The patient's history alone is sufficient to diagnose PCOS.
    d. Ultrasound findings do not contribute to the diagnosis of PCOS.
    e. Menses occurring every 28 days.

6. A 27-year-old woman is thought to have an endometrioma on ultrasound before an IVF cycle. Which one of the following is a true statement about endometriomas in patients undergoing IVF?

    a. Endometriomas do not affect the number of eggs retrieved in an IVF cycle.
    b. Blood flow in endometriomas is generally central in location when evaluated by Doppler.
    c. The presence of endometriomas is associated with a markedly reduced pregnancy rate after IVF.
    d. One ultrasound finding with endometriomas is the presence of "kissing ovaries" or ovaries stuck together in the cul-de-sac.
    e. Endometriomas are echolucent and have the same echo pattern as ovarian follicles.