

# Cervical Barriers: Adjuncts to Microbicides

# Cervix: Site of High Susceptibility

- Pregnancy
- Classical cervicotropic STDs (CT, GC)
- HIV
- Other cell-associated viruses
  - CMV, HTLV I, HTLV II
- Other systemic viruses
  - Hepatitis B, Hepatitis C
- Herpes and papillomaviruses

# Cervical Exposure Sites



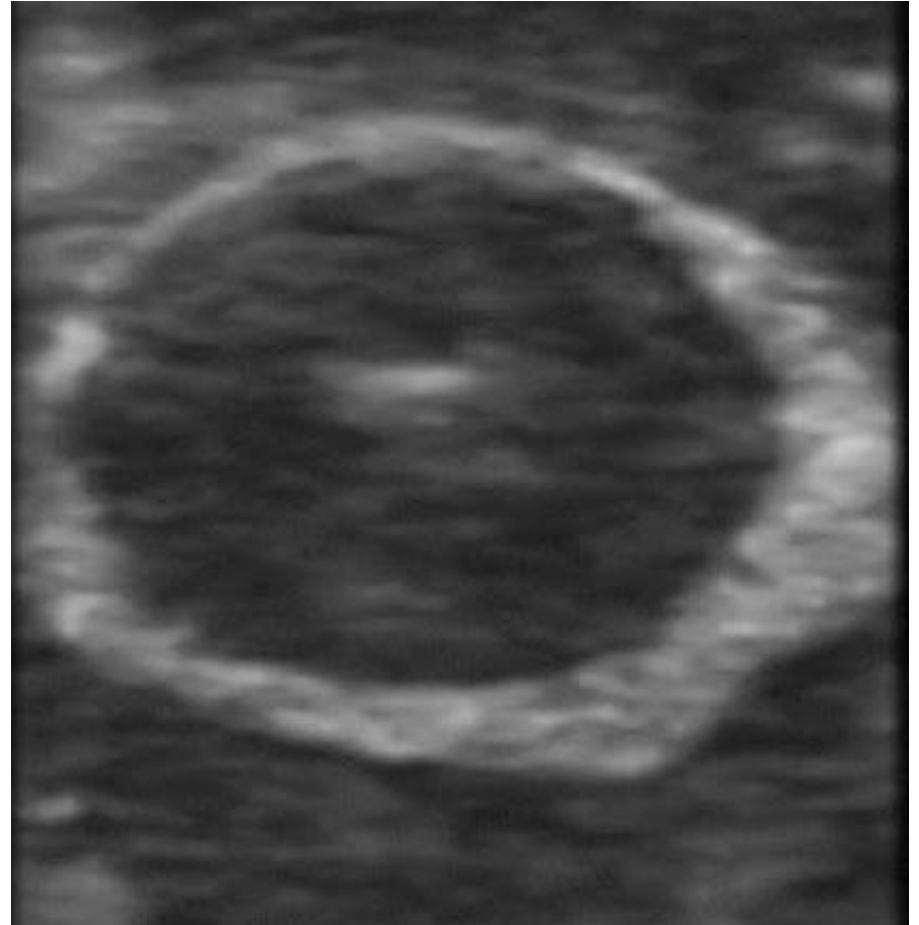
Bollen LJM, Kilmarx PH, Wiwatwongwana P. Photo Atlas for Microbicide Evaluation [CD-ROM]. Bangkok: Thailand MOPH - U.S. CDC Collaboration; 2002.

Is The Upper Tract Exposed?

# Kadanali et al., Contraception 2000

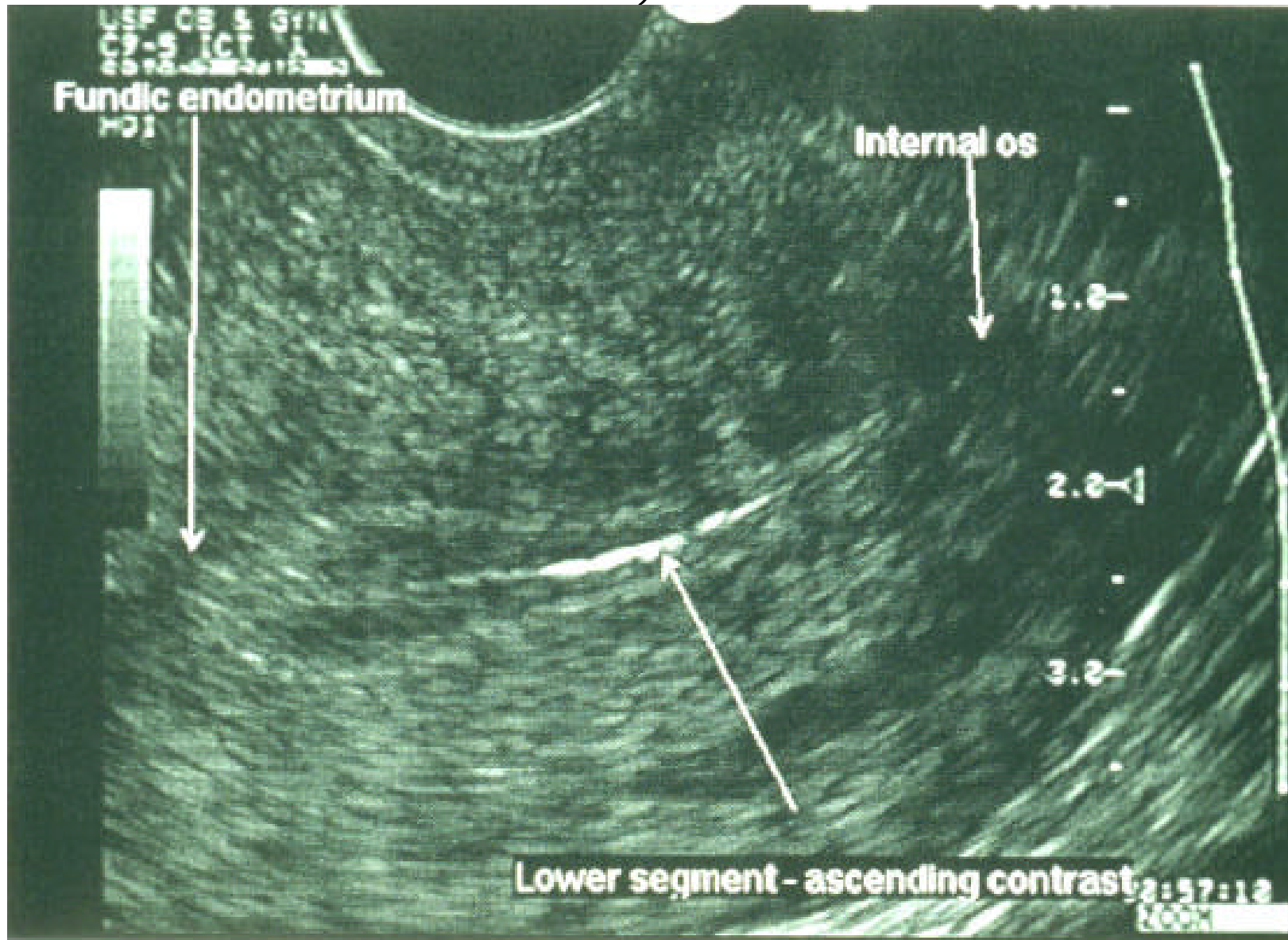


Barnhart, Stolpen, Pretorius, and Malamud, 2001  
MRI with Contrast-Labeled Microbicide



# Contrast Ultrasonography

Dr. Anna Parsons, U of S. Florida



# Uterine Peristalsis, No Contrast

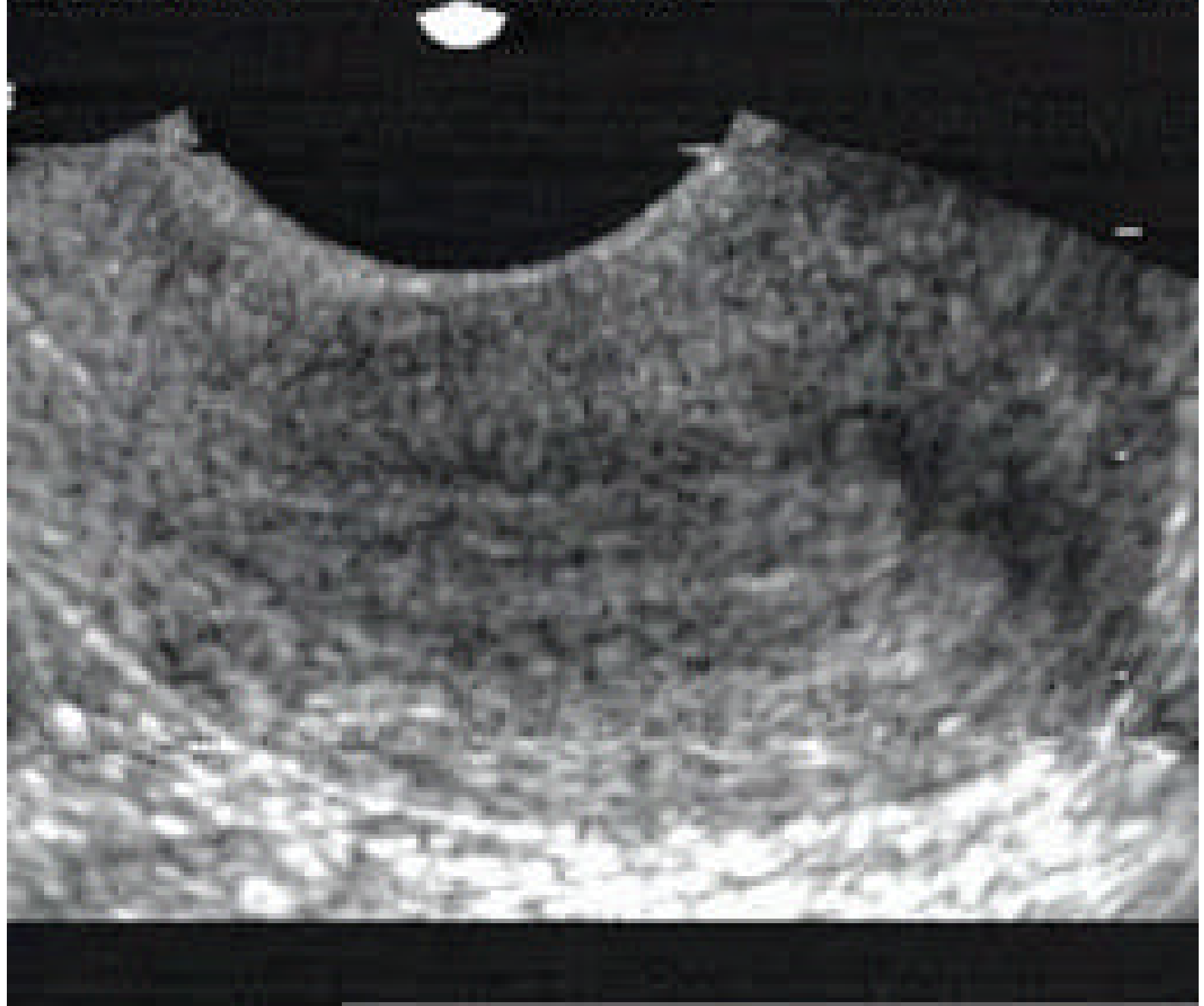


Age-Based GYN

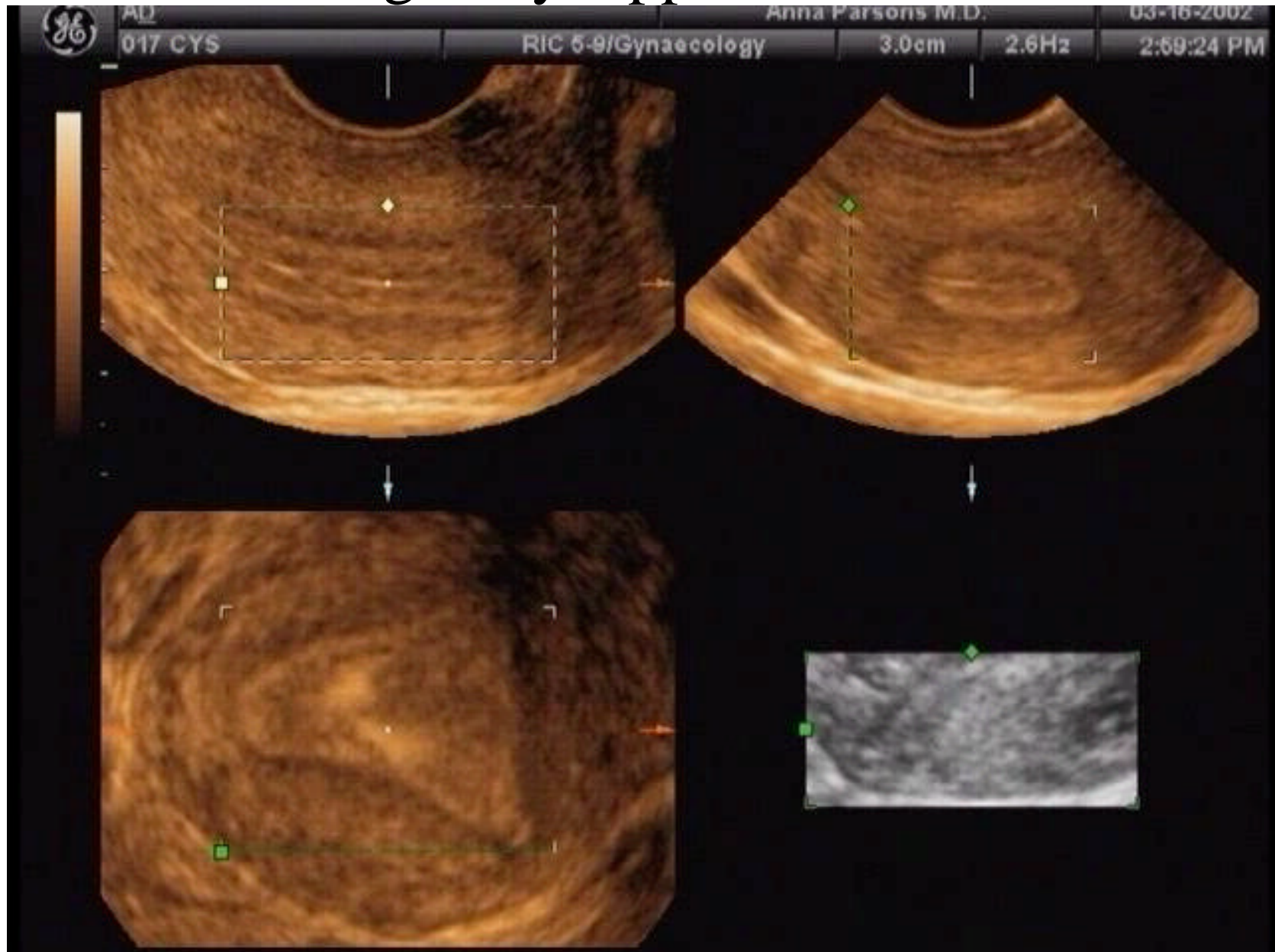
OB-Gyn GynFertPel

15:37:33

20 Hz



# Persistaltic Uptake of Vaginally Applied Contrast





AD  
017\_CYS

RIC 5-9/Gynaecology

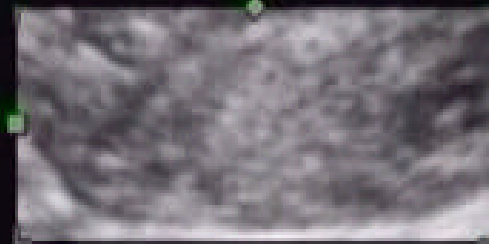
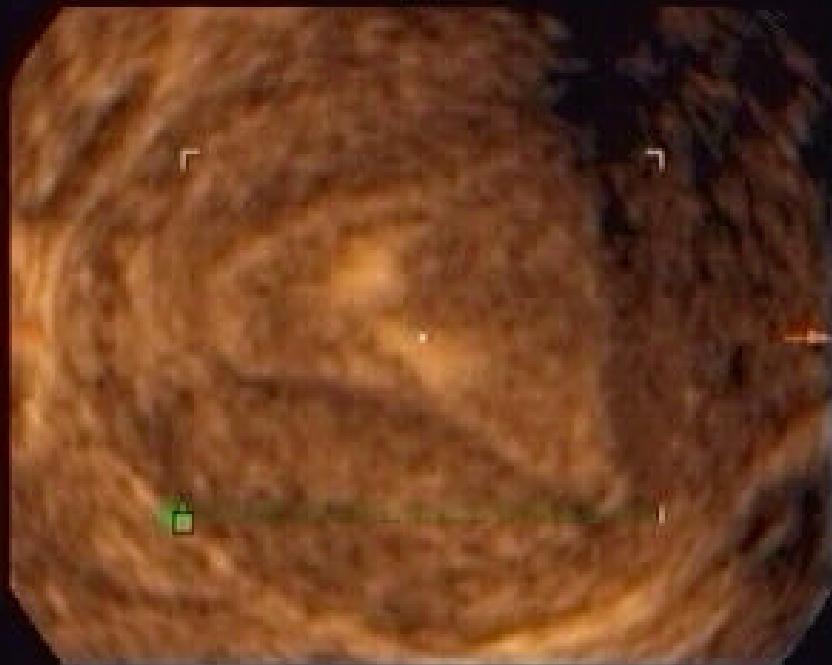
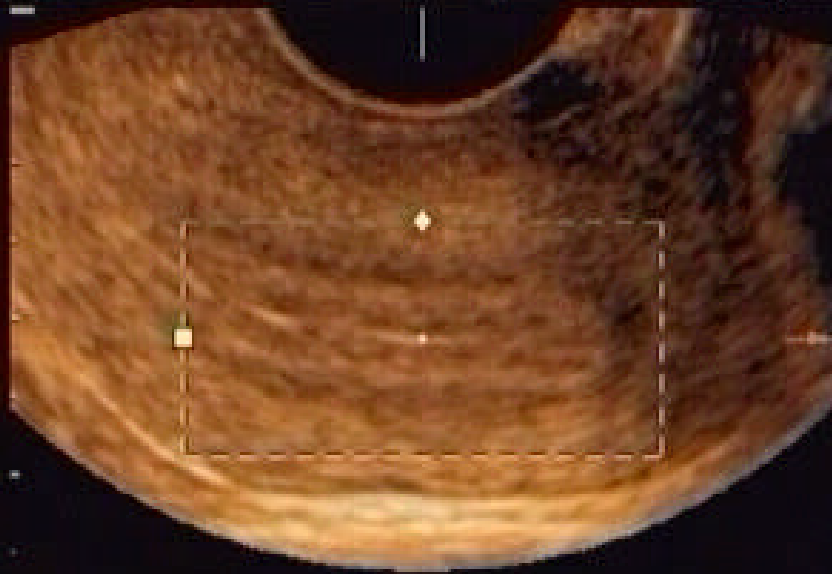
Anna Parsons M.D.

03-18-2002

3.0cm

2.6Hz

2:59:24 PM



# Summary of Sonography Studies

- Uterine uptake of vaginal fluid was observed in 17 of 20 women
  - 17 to lower uterine segment
  - 13 also to fundus
  - 3 also to one or both intramural tubes
- Using contrast as tracer, ascent of semen documented (in 4 of 4 midcycle women)
- Results with cervical barrier device:
  - Contrast placed on vaginal side detected on cervical side in 2 of 4 studies, and subsequently ascended to uterus in both

# Why Not Rely on Microbicide Alone? What would barrier add?



**Why Not Use Cervical Barrier Alone?**

# Are Cervical Barriers Used Alone Effective? (Contraception)

## Studies of devices without spermicide

### – Diaphragm

			Pregnancy Rate ( <u>pregnancy/100 woman years</u> )
• Stim '80	continuous wear,	60 mm	1
• Smith '95	continuous wear,	60 mm	24.1
• Bounds '95	intermittent wear,	fitted	28.6

### – Lea's shield

• Mauck '96	intermittent	1-size	20	(extrapolated from a 12.9% unadj. 6 mo. rate)
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**Conclusion:** Cervical barriers used alone have significant efficacy

- Probably comparable to spermicide used alone
- Diaphragm + spermicide probably more effective than diaphragm alone

# HIV Prevention Using Cervical Barrier Without Microbicide?

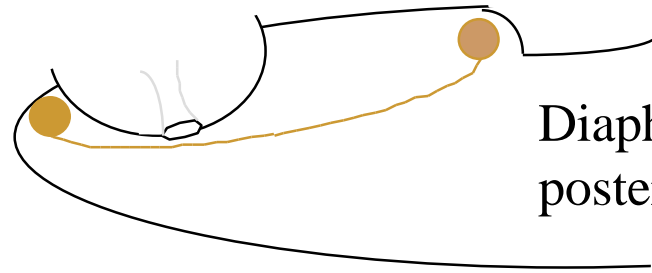
## Advantages:

- Simple
- Inexpensive
- No need for “consumables,” – improved logistics
- No need for investigational drug

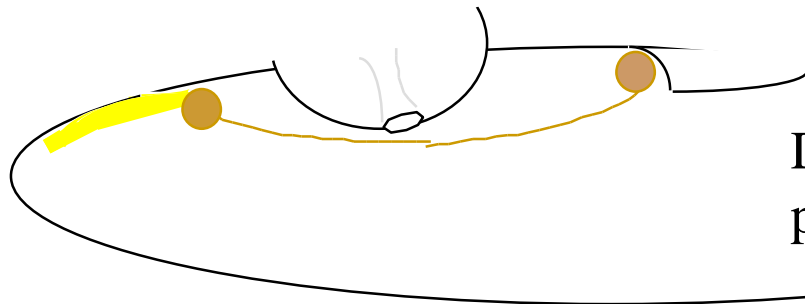
# HIV Prevention with Bare Diaphragm?

## Limitations

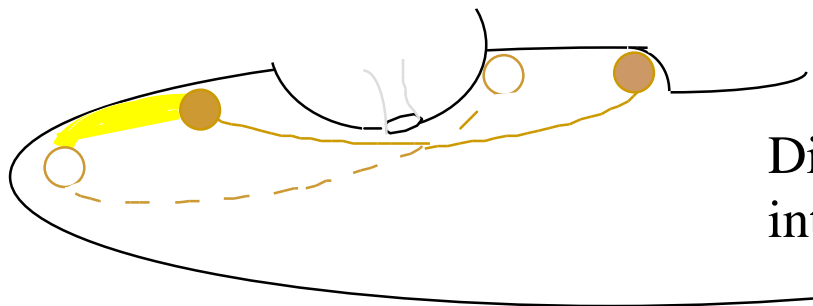
- No protection for vagina
- Protection of cervix likely to be incomplete:
  - Barriers act as baffles (partial barriers) not hermetic seals
    - Vaginal folds compromise seal
    - Devices move during intercourse



Diaphragm “press fit” between posterior fornix and pelvic brim



During intercourse posterior fornix elongates



Diaphragm movements during intercourse diminish barrier function

# Baffle (partial barrier) Concept

- Hermetic seal?
  - Unattainable
  - Unnecessary
- With barrier + microbicide, even a partial barrier assures mixing of microbicide and semen before semen contacts cervix

# Options for Cervical Barrier Trials:

- Bare cervical barrier
- Cervical barrier with bland lubricant gel (e.g. KY)
- Cervical barrier with possibly active gel (e.g.Replens)
- Cervical barrier with active microbicide
- Cervical barrier with active microbicide on both sides

Increasing Efficacy ↓

Increasing Complexity ↓

# Redundancy Reduces Risk of a Failed Trial

**ACTG 076 success** (blocking mother to infant transmission)

- Rx mother with oral AZT for last two trimesters
- Rx mother continuous i.v. AZT during labor
- Rx infant for 6 weeks postpartum

**Generalization: Employ redundancy when:**

- Mechanisms and optimal approach still unknown
- No proof-of-principle in hand, and an early success badly needed
- Failure would be catastrophic

# Summary

- The cervix is hot spot for pregnancy, CT, GC, transmission, and probably HIV and several other STDs.
- Cervical barriers used alone are effective in preventing pregnancy, and give similar efficacy to spermicides alone.
- When used with barrier devices, spermicides appear to increase contraceptive effectiveness.

# Summary (continued)

## Cervical barriers:

- will likely offer STD/HIV protection
- will likely improved the efficacy of microbicides compared to microbicides used alone
- promise best protection when used *with* microbicide especially if the microbicide is delivered to both the cervical and vaginal sides