Impact of Uterine Anomalies on fertility potential ;

Review of the literature....

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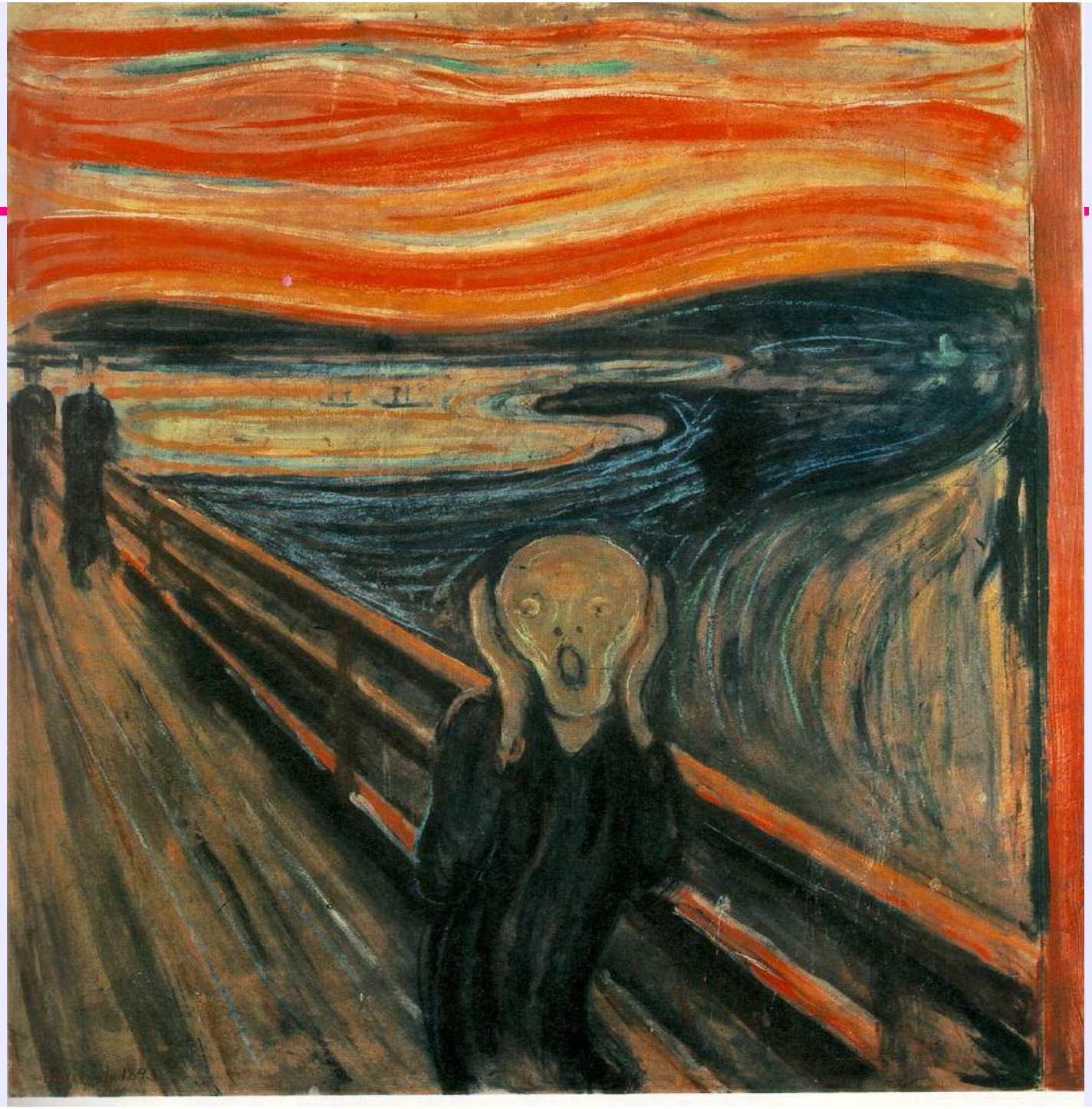
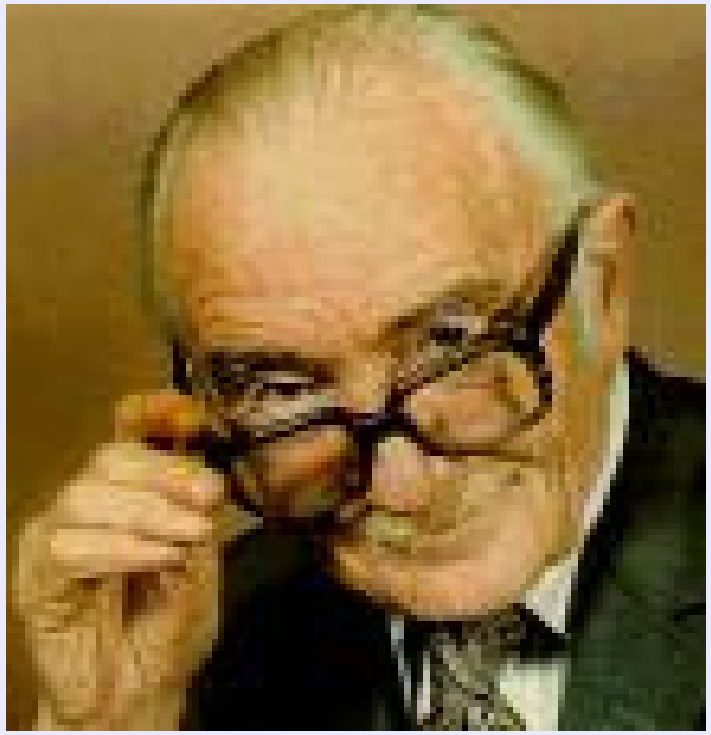
ESHRE Mtg Manchester 20th Nov 2009



Presentation

- Dysmenorrhoea
- **Subfertility**
- **Recurrent pregnancy loss**
- Preterm Delivery

Evidence Based Medicine



Archie Cochrane

- What evidence do we have ?
- Always difficult in surgical trials…..

Evidence ????

- debate over which diagnostic tests
- debate over accuracy of diagnosis
- debate on prevalence.. And which control groups were used
- debate over what is a problem ..or not
- different surgical methods of treatment
- Infertilty ; multifactorial
- confounding factors ; 'PCO more common in pts with Mullerian abnormalities' *Ugur et al 1995*
- Endometriosis more common in pts with septate uteri

- So do we have any robust evidence at all ?

Is there good evidence .....

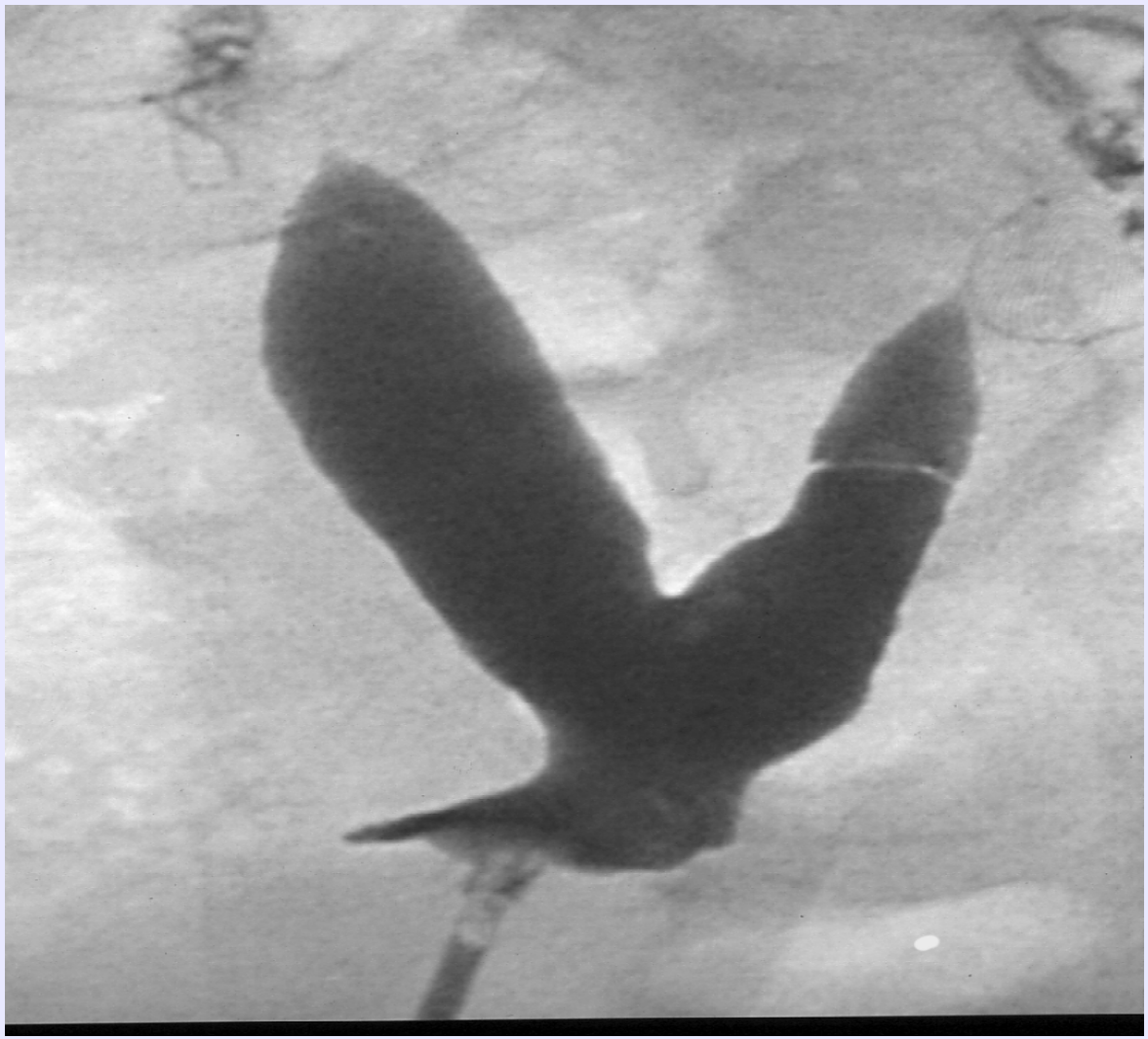
- **Pregnancy outcomes?**
- **Infertility ?**

Evidence

- **Not much !**

- **Review of the literature**
- **Extraction of what evidence there is**
- **Application of this evidence**
- ***Common sense / pragmatic approach***

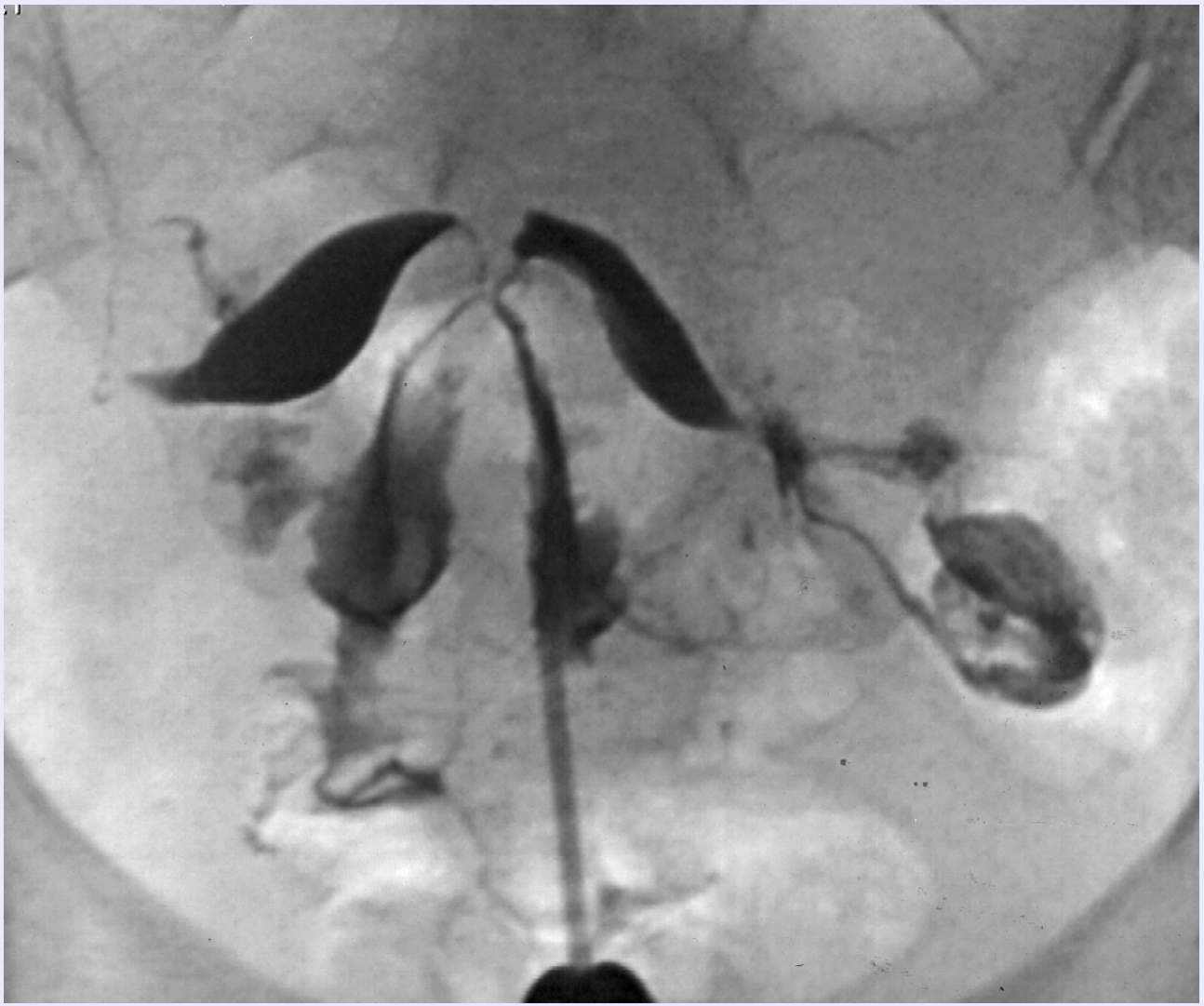
HSG Septate uterus



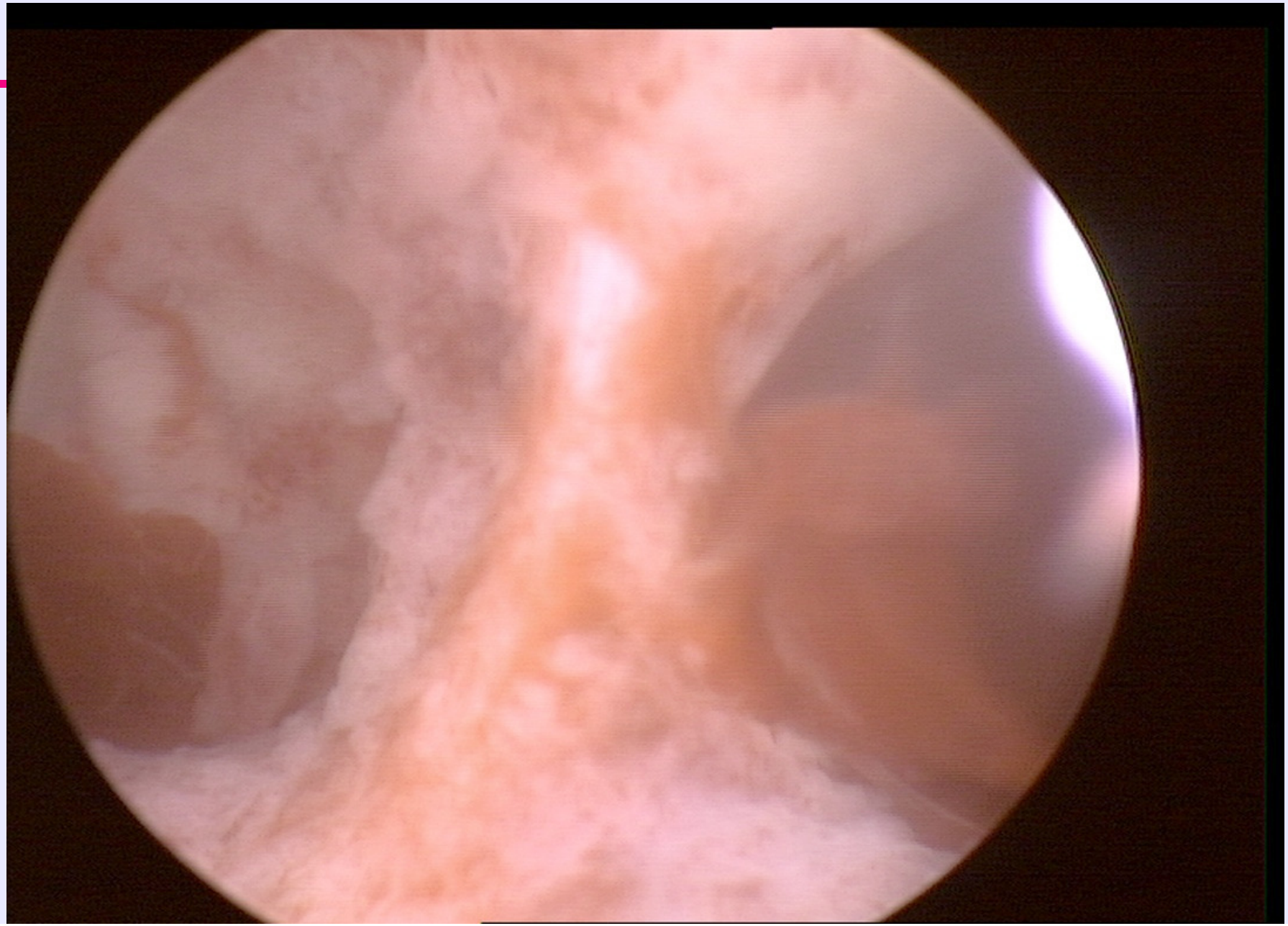
HSG ? Septate Uterus

HSG ? Bicornuate

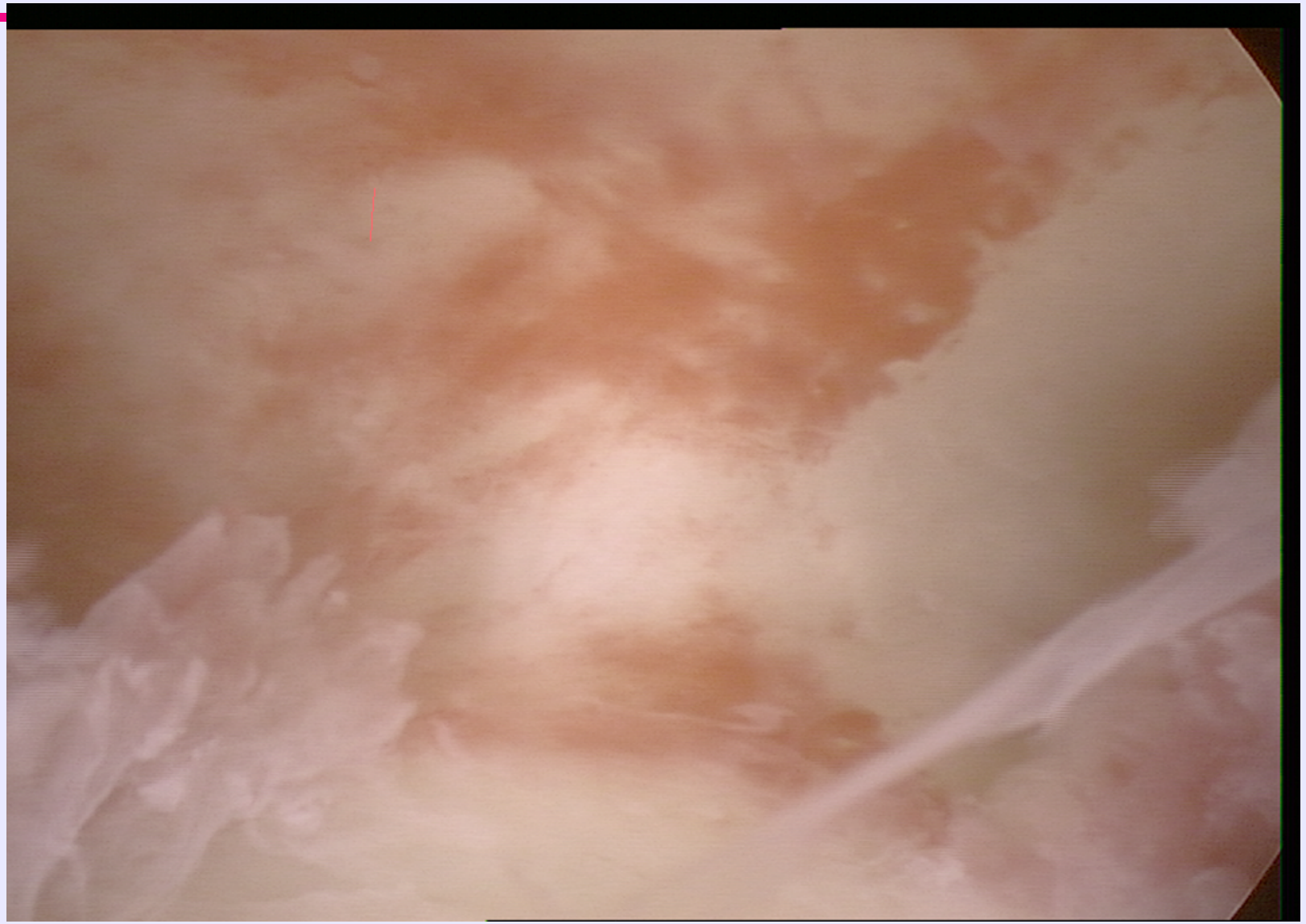
HSG Didelphic Uterus



Uterine Septum



? Uterine Septum



Prevalence....

- **The prevalence of congenital uterine anomalies in women with reproductive failure remains unclear, largely due to methodological bias.....**

Saravelos SH, Cocksedge KA, and Li TC

Human reproduction update 14(5):415-29, 2008

Diagnosis...

- Clinical examination
- HSG's
- 2-D ultrasound
- 3-D Ultrasound
- HyCoSy
- MRI
- **Laparoscopy & Hysteroscopy**

Prevalence ‘Control group’

- patients with other gynaecological problems
- Laparoscopic sterilisation

Etc.....

Effect on congental uterine anomalies on adverse *pregnancy outcome* ....

well recognised

- Grimbizis GF, Camus M, Tarlatzis BC, Bontis JN, Devroey P Clinical implications of uterine malformations and hysteroscopic treatment results. Hum Reprod Update 2001; 7:161–174.
- Raga F, Bauset C, Remohi J, et al. Reproductive impact of congenital mullerian anomalies. Hum Reprod 1997; 12:2277–2281.
- Acien P. Reproductive performance of women with uterine malformations. Hum Reprod 1993;8:122–126.
- Patton PE. Anatomic uterine defects. Clin Obstet Gynecol 1994;37:705–721.
- Homer HA, Li TC, Cooke ID. The septate uterus: a review of management and reproductive outcome. Fertil Steril 2000;73:1–14.
- Kupesic S. Clinical implications of sonographic detection of uterine anomalies for reproductive outcome. Ultrasound Obstet Gynecol 2001;18:387–400.
- Taylor E, Gomel V. The uterus and fertility. Fertil Steril 2008;89:1–16

Effect on *fertility* less so.....

- Grimbizis GF, Camus M, Tarlatzis BC, Bontis JN, Devroey P Clinical implications of uterine malformations and hysteroscopic treatment results. Hum Reprod Update 2001; 7:161–174
- Kupesic S. Clinical implications of sonographic detection of uterine anomalies for reproductive outcome. Ultrasound Obstet Gynecol 2001;18:387–400.
- Taylor E, Gomel V. The uterus and fertility. Fertil Steril 2008;89:1–16.
- Heinonen PK, Pystynen PP. Primary infertility and uterine anomalies. Fertil Steril 1983;40:311–316.
- Sanders B. Uterine factors and infertility. J Reprod Med 2006;51:169–176

Do congenital anomalies have an effect on infertility ?

- **Potential mechanisms**
- **Possible associations**
- **Probable underlying causation**

Potential mechanisms

... Whereby congenital anomalies may exert an effect

- Uterine musculature / fibrotic areas
- Effect on endometrium
- Uterine vascularity
- Uterine contractility
- Uterine receptivity
- Increasing other pathology – endometriosis ?

Possible associations

- exist if the prevalence of congenital anomalies was greater in the infertile group compared with fertile

Or

- Infertility more likely amongst those that have these anomalies

But

- Prevalence
- Diagnosis... Again...

Probable underlying causation

- *cause-effect relationship*
- **The presence of these anomalies leads to infertility**
- **Consequently *treating* the anomaly would lead to an improvement in fertiltiy**

Prevalence

	Nahum	Acien	Grimbizis
	1998	*1997*	*2001*
Arcuate	**7%**	**15%**	**20%**
Septate	**34%**	**22%**	**35%**
Bicornuate	**39%**	**46%**	**25%**
Unicornuate	**5%**	**4.5%**	**10%**
Didelphic	**11%**	**11%**	**8%**
Other	**4%**	**4%**	**3%**

Association **Prevalence**

Nahum 1998 ; 6512 infertile women

- **3.5% prevalence of CUA in the infertile group**
- **0.17% in the fertile group – x20 higher**

Grimbizis 2001 ; 3600 infertile women

- **3.4% in CUA group**
- **4.3% in general population**
- **Different population groups / different diagnostic criteria...**

Saravelos 2005; prevalence higher in infertile group versus general 8.1% v 4.6%

Arcuate uterus

- Is it a fertility problem?
- Do you treat it?

Diagnosis

- Arcuate uterus considered by many to be a normal variant
- ? Not reported
- ? Not operated on
- Raga et al 1997 ...'no impact on reproduction'

Cause - effect - correction

- ‘strong’ evidence for hysteroscopic metroplasty in poor reporoductive outcome groups
- miscarriage rates down from 88% to 14%
- 80% of women will have a term delivery after metroplasty compared to 3% before

Grimbizis 2001, Homer 2000, Taylor 2008, Kupesic 2001

Cause - effect - correction

- for primary infertility – more controversial!
- may benefit ;
- Fayez 1986, Perino et al 1987, Daly et al 1989,, Fedele 1993

But

- Goldenberg et al 1995 ; metroplasty didn't seem to make any difference
- Surgical technique??
- Other co-existent pathology ??

Treatment

Do

They

Need

It !!

When do you operate ?

Uterine Abnormality

- **20 - 25% of women will experience reproductive problems**

Rock & Jones Fertil Steril 1977 ; 28:798

Buttram & Gibbons Fertil Steril 1979 ; 32(1) : 40 - 46

Cause – effect - treatment

Some evidence.....

The outcome of singleton pregnancies after IVF/ICSI in women before & after hystx resection of a uterine septum compared to normal controls

- **Large septum & small partial septum compared to matched controls**
- **Abortion rate before resection significantly higher than controls – both groups**
- **78.8 v 23.7% - small septum ; 83.3 v 16.7% - large septum**
- ***After surgery abortion rates comparable in both groups***

Conclusion – both large and small uterine septae are an important & hysteroscopically preventable risk factor for spontaneous pregnancies in patients after IVF & ICSI

Ban Frangez et al , Eur J Obstet Gynecol Reprod Biol June 2008

- **Controversial !**
- **“although uterine septum does not cause infertility….”**

Sui L et al, Surg Endosc Sept 2009

Reproductive outcome following hystx metroplasty in women with complete septum, double cervix & vagina

- **Compared to untreated women with same pathology**
- **Cycle fecundity better ($p = 0.046$)**
- **Term delivery rate significantly improved ($p < 0.05$)**
- **Rate of spontaneous abortion significantly decreased ($p < 0.05$)**

Lin K et al, Int J Gynecol Obstet April 2009

Hysteroscopic resection of the septum improves the pregnancy rate of women with unexplained infertility ; a prospective controlled trial

- to assess fecundity of infertile women after surgical correction of septum
- Group A ; septum + unexplained infertility
- Group B ; unexplained infertility alone
- Gp A – operated : Gp B - managed expectantly
- Both groups followed up for a year
- pregnancy rate (38.6 v 20.4%) & live birth rate (34.1 v 18.9%) both significantly higher in group A

Mollo A et al, Fertil steril May 2009

Conclusion I

- not all women with CUA are infertile
- there is an *association* between infertility and CUA
- There is an impact on reproductive outcome
- Most CUA are not suitable / ameniable to surgery
- Some patients with septate uteri may benefit from a *well performed* hysteroscopic metroplasty
- Thorough investigations for co-existent pathology must be performed

Conclusion II

- The CUA must be looked at in the entirety of the couple
- The patients history must be considered
- the reproductive outcome as well as the fertility impact must be considered
- All options and outcomes must be discussed with the patients.

Thank you...

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