

Current Evidence On Infertility Treatment

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Problem of Infertility

- It is a state in which a couple , desirous of a child, cannot conceive after 12 months of unprotected intercourse.
- One out of six to seven couples seeks medical advice for an infertility problem.
- It may be unexplained ; when no cause could be detected (incidence 8-28%).

Problem of Infertility (cont.)

- Treatment of infertility/ subfertility has changed in the last 2 decades due to higher technological development and appearance of advanced sets of diagnostic and therapeutic modalities.
- Unfortunately, most of treatment modalities are not based on sound clinical evidence

Problem of Infertility (cont.)

- The increase in the demand for treatment appears to be generated by greater expectations and by the increased media focus on the new medical procedures and technologies available for achieving pregnancy.

Problem of Infertility (cont.)

- The role of the physician is to provide the couple with accurate information
- He should discuss with the couple the probabilities of the success of all available treatments that may work for their condition.

Study Design

- This overview aims at searching for the best evidence of effectiveness regarding various infertility therapies.
- An electronic search was made in:
 - Cochrane library, issue 1,2003.
 - Medline database using Ovid software for RCTs, and systematic reviews between 1997 and 2003.

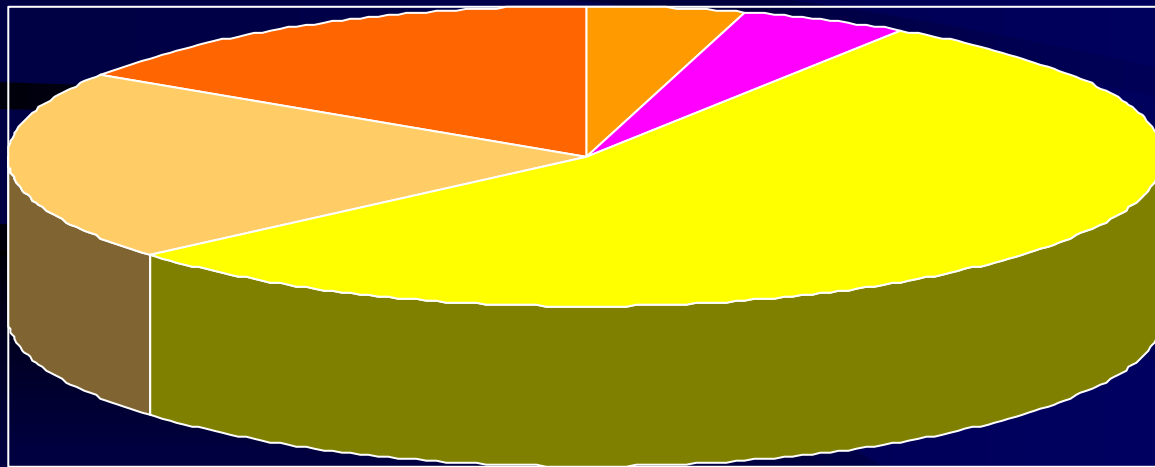
Study Design (cont.)

- The trials were then evaluated according to criteria adapted from *How to use an article about therapy or prevention.* (Guyatt et al, JAMA, 1994)
- The cochrane systematic reviews related to the search were selected.

Results

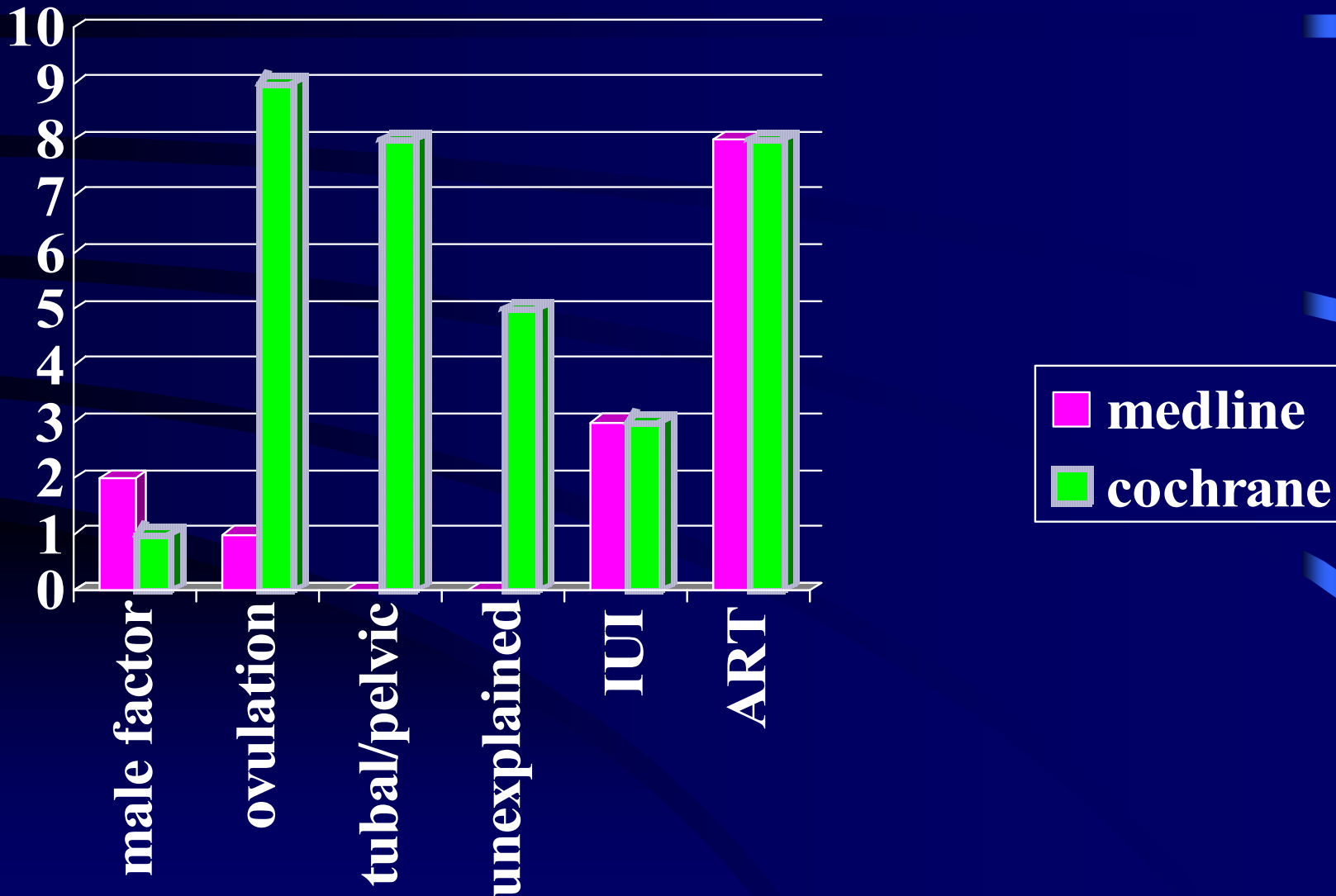
- The search retrieved 70 Cochrane systematic reviews; 34 of them are related to the overview.
- The medline search retrieved 109 trials; 14 of them were eligible.

Excluded Clinical Trials



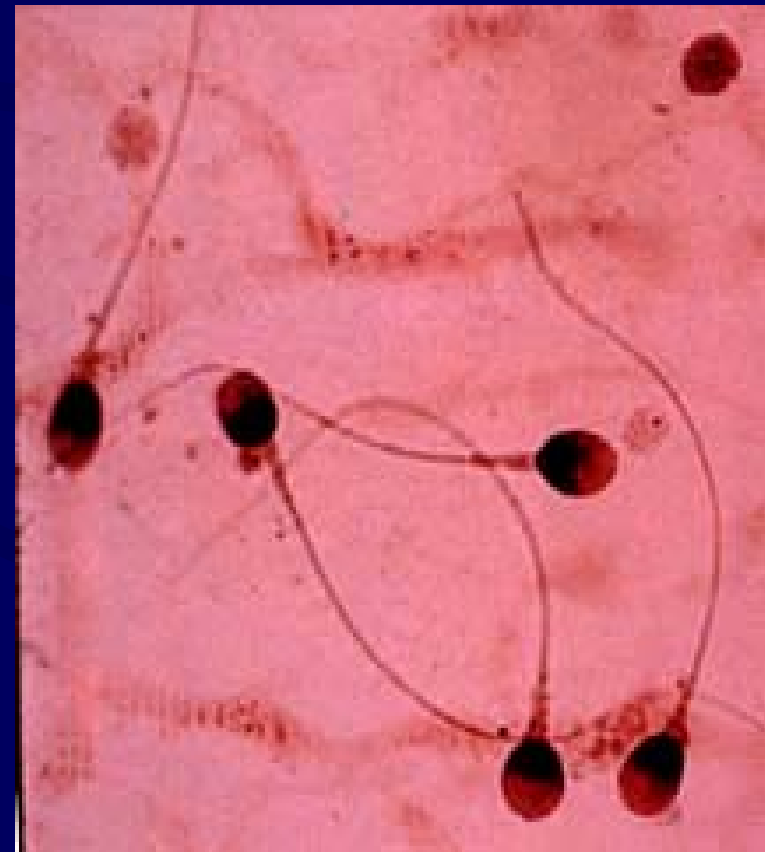
- poor design
- poor randomisation
- low power
- statis. Inconvenience
- unrelated

Distribution of the studies



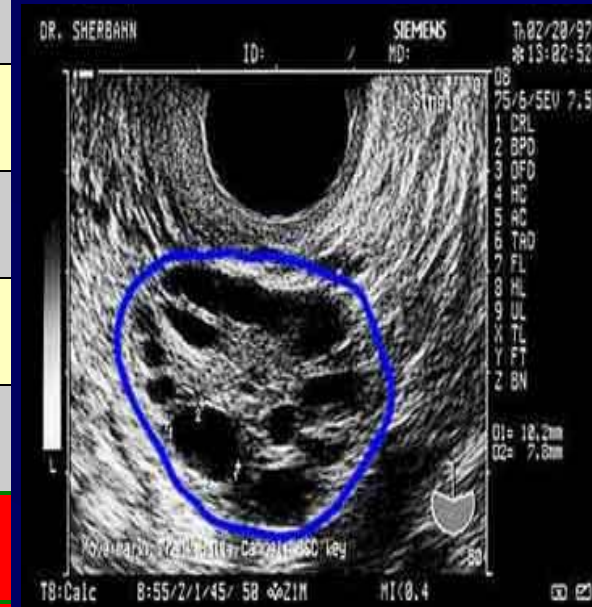
Male Infertility

- There is no evidence that treatment of varicocele in men from couples with otherwise unexplained infertility will improve the pregnancy rate .
- Administration of both zinc sulphate and folic acid increases total sperm count.



Polycystic Ovarian Syndrome

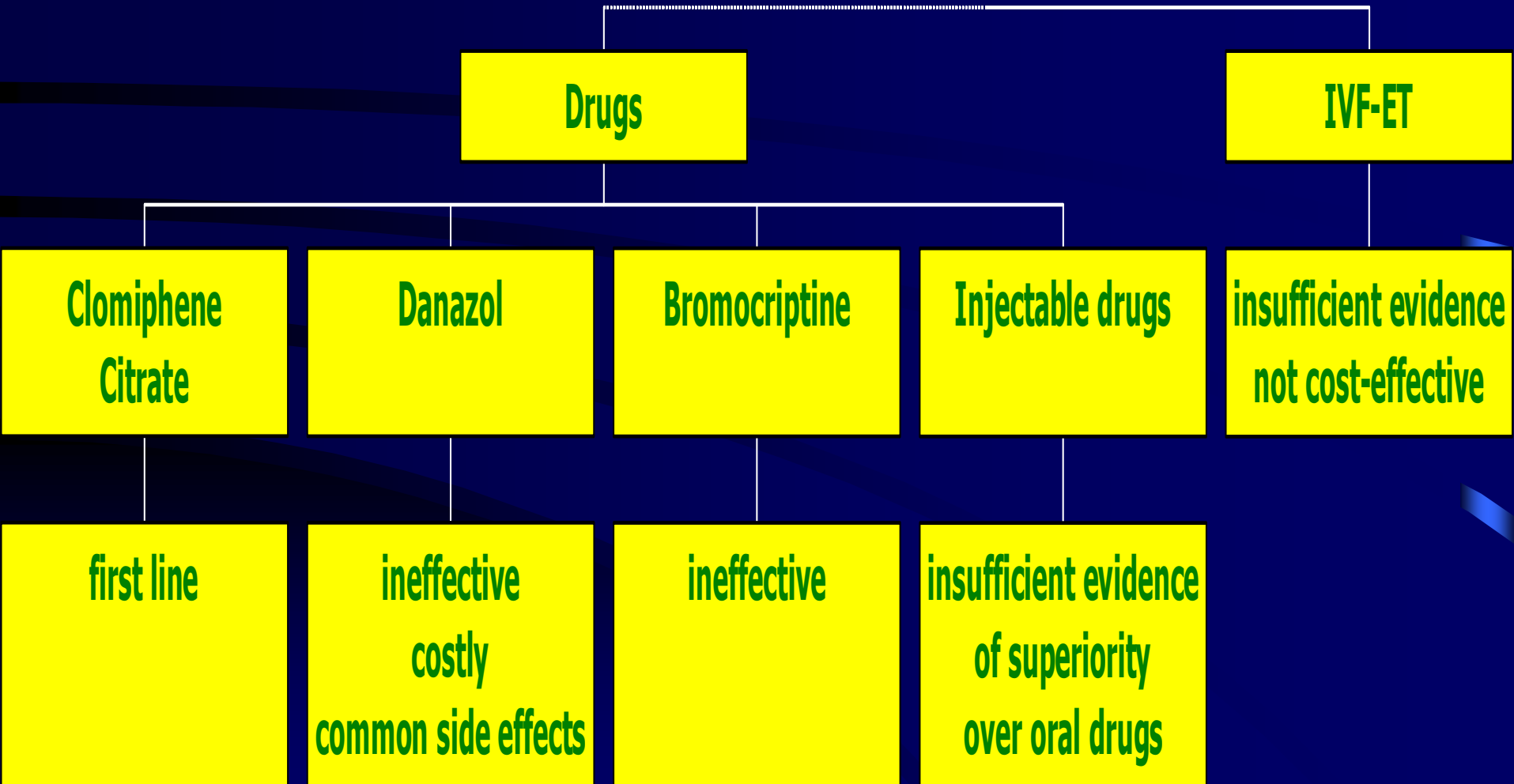
Intervention	Decision/ evidence
Use of CC	Effective
Gonadotrophins	No evidence
GnRH analogues	Ineffective
Metformin	No evidence
Pulsatile GnRH	No evidence
Ovarian drilling	No evidence



Endometriosis

- Laparoscopic surgery : may improve pregnancy rate if used for minimal or mild disease (evidence not clear)
- Ovulation suppression: showed no benefit + side effects
- Use of GnRH agonists before IVF-ET increases pregnancy rate

Unexplained Infertility



Intrauterine Insemination

- CC is a good alternative to hMG before IUI
- IUI seems to be better than timed intercourse
- No benefit of double compared to single IUI per cycle
- Ten minutes rest after IUI improves pregnancy rates.

ART

- COH
 - GnRH antagonist beneficial over GnRH agonist
 - No evidence in favour of either hMG, FSH.
 - rFSH+CC= long protocol
 - Growth hormone: ineffective
- Prevention OHS
 - IV albumin: beneficial effects shown
 - Coasting: No evidence available
 - Embryo freezing: No evidence available

ART

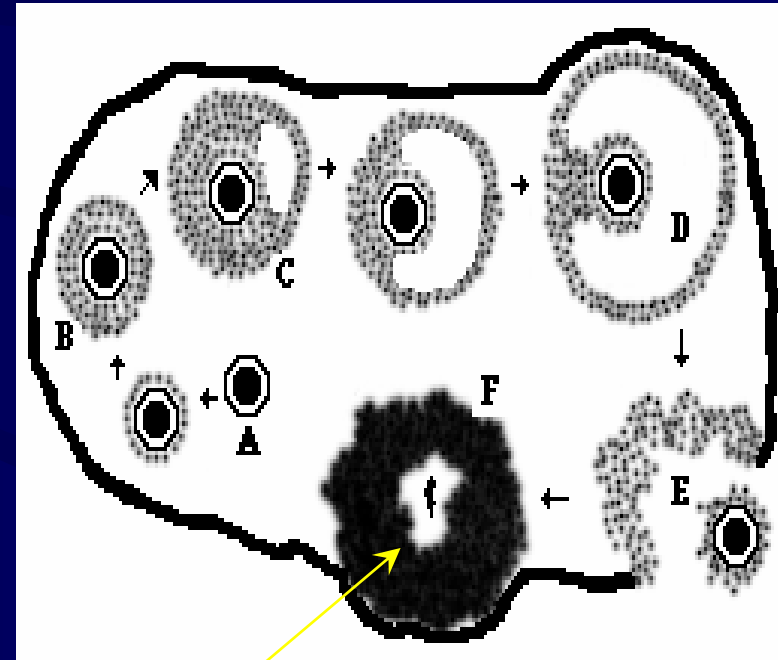
Sperm Manipulations

- Cryo preservation has no deleterious effect on the pregnancy rate in ICSI .
- Clear evidence of superiority of ICSI over conventional IVF in cases with borderline semen parameters. In male with normal semen , this is less evident. ICSI should be reserved only for cases with abnormal semen parameters.

ART

Luteal Phase support

- There is a clear evidence that progesterone or hCG I.M. is better than no treatment.
- Progesterone is safer than hCG to avoid the risk of OHS.



Conclusions

- Infertility can be a hard road , both emotionally and financially.
- There is a plethora of infertility therapeutic modalities.
- Emotional aspect should be considered while managing infertile couple.
- There are 3 groups of interventions (according to evidence) :

Conclusions (cont.)

A - *Good* evidence of effectiveness:

- 1 - Use of CC in PCOS patients.
- 2 - Use of GnRH antagonists in ART.
- 3 - Use of r-hCG in final maturation of the oocyte.
- 4 - Use of IV albumin to prevent OHS.
- 5 - Use of ICSI in borderline semen.
- 6 - Support of luteal phase by progesterone.
- 7 - Use of GnRH-a in endometriosis before IVF.

Conclusions (cont.)

B - *Good* evidence of *ineffectiveness*:

- 1 - Varicocelectomy .
- 2 - Use of uFSH, GnRH analogues in PCOS patients.
- 3 - Use of depot GnRH , growth hormone in ART.
- 3 - Use of ICSI for normal semen.
- 5 - Use of danazol / bromocriptine for unexplained infertility.
- 6 - Use of ovulation suppression in endometriosis before IVF.

Conclusions (cont.)

C - *Lack of* evidence : examples ;

1 - Zinc & folic acid for abnormal semen

2 - PCOS patients :

Use of pulsatile GnRH

Use of metformin

Ovarian drilling

Use of Gonadotrophins

3 - ART program :

Use of rFSH Vs hMG

Embryo freezing

Conclusions (cont.)

- ❑- Low power was the main rejecting feature, this means that the forthcoming studies should be of sufficient sample size.
- ❑- Only few treatment lines have been described as either effective or ineffective. The majority are still in the gray zone.
- ❑- ART outcome should be measured in terms of single live birth per cycle.

Conclusions (cont.)

- ❑ Cost-effectiveness should be scrutinised because infertility treatment options may be dictated by economical considerations rather than by medical effectiveness.
- ❑ In order to establish a cost-effective care, clinical outcomes under various cost conditions have to be examined.