Prof. Dr. Abha Majumdar
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INDIA

'President's Medal' for *best medical graduate 1970-75.*
'Dr. B.C Roy's award' in 1999 for *outstanding contribution towards medicine and field of specialty,*
'Vikas Ratan Award' by *Nations economic development & growth society 2002*
'Chitsa Ratan Award' by the *International Study Circle , 2007*
Felicitated by Agra medical college for '*Outstanding contribution towards field of speciality. 2008*
Appointed by National Board of Examination as course director to award post doctoral **Fellowship in Reproductive Medicine since** 2007, and by FOGSI for basic as well as advanced infertility training since 2008
Member of Editorial board of '**Worldwide IVF**' and peer reviewer for '**Journal of Human Reproductive Sciences**'
Over 15 publications in indexed journals and 20 chapters in textbooks for ob/gyn and reproductive medicine and delivered more than 150 guest lectures and orations in national and international conferences.
She has been in the team of doctors responsible for the first IVF baby born in 1991 and the first frozen oocyte baby born in 2009 in Northern India

Abnormal semen analysis what next?.....

WHO SEMEN ANALYSIS 2010

Parameter	Lower reference limits (WHO 2010)
Volume (ml)	1.5
Total sperm number (10^6 per ejaculate)	39
Sperm concentration (10^6 per ml)	15
Total motility (%)	40
Progressive motility (%)	32
Vitality (live spermatozoa, %)	58
Sperm morphology (normal forms, %)	4
pH	>7.2
Peroxidase-positive leukocytes (10^6 per ml)	<1.0

Evaluation Of Abnormal Semen Analysis

- 2 Semen Analysis 3 weeks apart
- Confirm Azoospermia by centrifugation of a semen sample at 3,000 g *15 minutes and high powered microscopic examination of the pellet .
- Detailed history and physical examination
- Hormonal evaluation (FSH, LH, total Testosterone, Prolactin)

Severe OATS or Azoo-spermia

- **Genetic profile**
  - ❑Karyotype for Klinefelters syndrome
  - ❑ Y chromosome micro-deletions
  - ❑ Cystic fibrosis gene mutations (CABVD)
- **Imaging**
  - ❑Scrotal ultrasound and colour Doppler
  - ❑A trans-rectal ultrasound scan (TRUS)
- **Post-orgasmic urine analysis in low volume semen**
  - ❑Rule out retrograde ejaculation

Abnormal semen parameters

OATS

- O-oligo (count)
- A-astheno (motility)
- T-terato (shape)

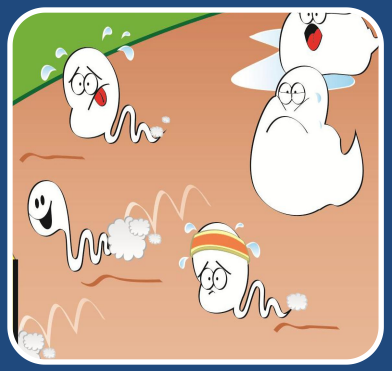
Azoo-spermia

- Obstruction in sperm passage
- No sperm production

Miscellaneous defects

- Low Volume
- High viscosity
- Genetically abnormal globozoosperm

Types of abnormal sperm parameters



OATS

- Mild
- Moderate

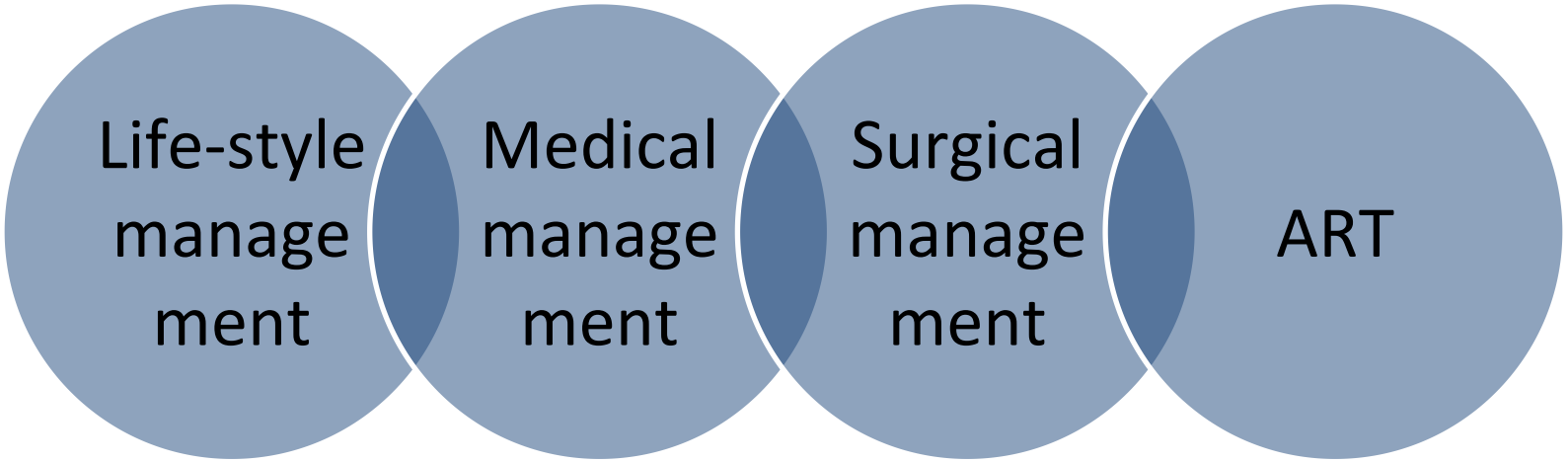
Azoo-spermia

- Hypogonadotropic hypogonadism
- Testicular failure

Miscellaneous

- Low volume / Retrograde ejaculation
- High viscosity

Treatment of male factor



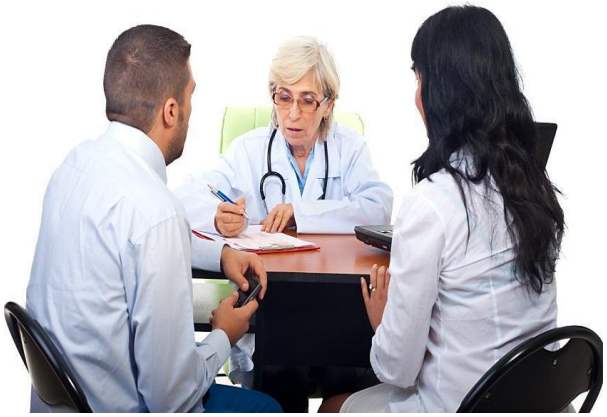
Lifestyle management

- Weight reduction for obesity
- Decrease alcohol & smoking
- Loose fitted undergarments
- Avoid occupational exposure to heat, frequent sauna or hot tub use,
- Avoid anabolic steroids
- Control diabetes

Medical management

Specific therapy

- **Hypogonadotropic hypogonadism**
- **Genito-urinary infections**



Non-specific therapy

- **Empirical treatment for Idiopathic OATS**

May help therapy

- **AROMATASE INHIBITORS** obesity
- **ANTOXIDANTS** High ROS

Specific therapy

Hypo-gonadotropic hypogonadism

Clinical Features	Investigations	Causes
• Low virilization • Hypotrophic testes • Azoospermia	• Low FSH, LH and Testosterone	• **Congenital:** Kallman synd Prader-Willi • **Acquired:** Pituitary tumor

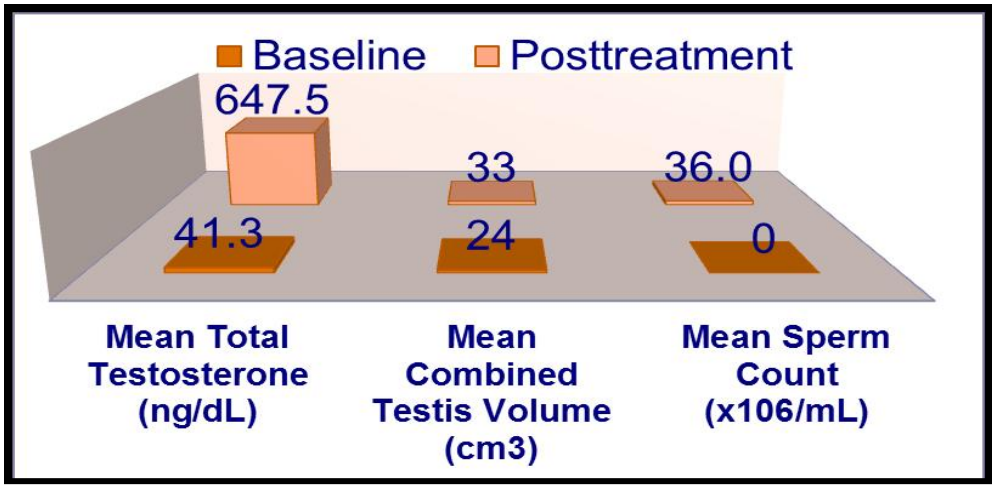
- ❑hCG (1500-2000 IU) I/M 2 to 3 times a week X 3mth
- ❑FSH injections 75 to 150 iu alternate day - 6-24 mths

Han TS et al , Clinical Endocrinology 2010;72(June (6)):731—7

Hypogonadotropic hypogonadism

Testicular growth in almost all and spermatogenesis in 80—95% of patients without undescended testes

Han TS et al , Clinical Endocrinology 2010;72(June (6)):731—7.



Esteves SC, Papanikolaou V; Fertil Steril 2011; Vol 96: S230

Infections of genito-urinary tract prostato-vesiculitis/MAGI

- Antimicrobial therapy - pyospermia ≥10 /ml of peroxidase positive WBC's X 6-12 weeks
- Only eradicates microorganisms but cannot reverse functional deficits or anatomic and secretory dysfunctions *(Weidner W et al, Andrologia 2008;40:105–12)*.

Men with leucocytes in semen: offer antibiotic treatment only if infection in genito urinary tract identified

Significance of anti-sperm antibodies unclear: effectiveness of systemic corticosteroids uncertain

Non specific therapy

Unexplained OATS

- No demonstrable cause for abnormal semen parameters
- ~30-45% of infertile men

WHO Laboratory Manual for the Examination of Human Semen and Sperm-Cervical Mucus Interaction. 4th edition. Cambridge (UK): Cambridge University Press, 2010.

Subnormal sperm parameters
sperm concentration ≤ 15million /ml
motility ≤ 40% motile sperm
normal morphology <4%

Unexplained OATS
Empirical drug treatment

- Androgens - contraindicated
- Low scientific evidence
  - Bromocriptine
  - hCG/HMG
  - α blockers
  - Systemic corticosteroids
  - Magnesium supplementation
  - Rec FSH and anti-oestrogens - beneficial in selected cases

Guidelines on Male Infertility. European Association of Urology 2012

Empirical medical Rx for unexplained OATS is in general **NOT EFFECTIVE**

Specific and Non-Specific Medical Treatment of Male Infertility

1. Little scientific evidence for empirical medical treatment in idiopathic (unexplained) male infertility.
2. Medical treatment only recommended in hypogonadotropic hypogonadism (GR-A)

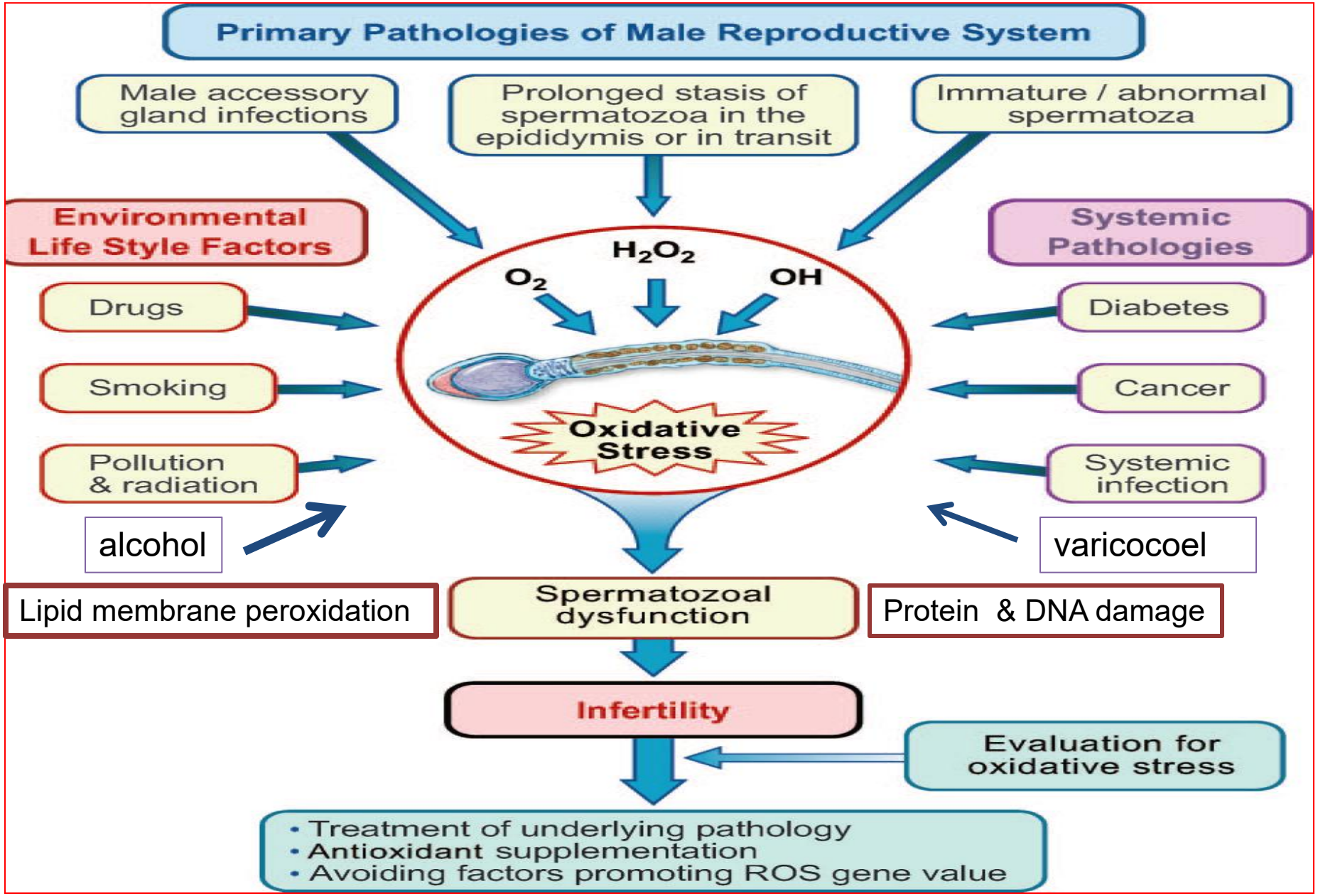
Specific and Non-Specific Medical Treatment of Male Infertility
Esteves 11

May help therapy

High levels of ROS

30%-80% of infertile men have elevated markers of OS in the form of reactive oxygen species (ROS)

Agarwal et al., Urology 2006



Factors contributing to oxidative stress-induced male infertility

Commonly used Antioxidants

- Vitamin E 400-600mg/day
- L-carnitine 3gm/day / L acetyl carnitine 3gm/day
- L-carnitine 2gm +L acetyl carnitine 1gm /day
- Co-enzyme Q 10 200mg to 300mg daily
- Ascorbic Acid 1000mg
- Zinc 200mg 2 times daily
- Selenium 200mcg/day
- Pentoxyphylline 1200mg/day
- Ethylcysteine 600mg/day
- N acetyl cysteine: 600mg/day

Oral Antioxidants

Cochrane Review 2011

Outcome	N studies	N participants	Effect size (OR; 95% CI)
Live birth	3	214	**4.85** [.92, 12.24]
Pregnancy rate	15	964	**4.18** [.65, 6.59]
DNA fragmentation	1	64	**-13.80** [-17.50, -10.10]
Miscarriage, sperm count, sperm motility	6-16	242-700	No effect
Adverse effects	6	426	No effect

Improve the outcomes of live birth and pregnancy rate for subfertile couples undergoing ART cycles

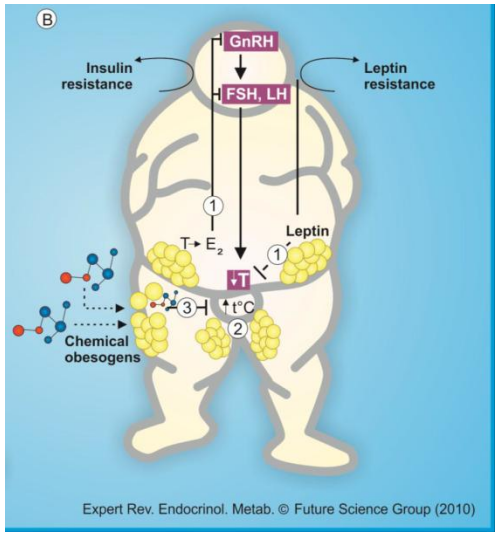
Oral antioxidants (OI)

1. Current evidence- OA supplementation for sub-fertile males improves chances for pregnancy and live birth for couples undergoing ART (Grade A)

Well-designed studies need to determine best candidates for OA therapy and which formulation and doses give better results.

Aromatase Inhibitors (AI)

- Obesity risk factor for male infertility (grade B)
- Peripheral androgen aromatization is enhanced in men with elevated BMI. Obese men show increased serum estradiol and low testosterone levels (grade-A)
- Lowering E2 levels by AI, increases LH and FSH levels by pit modulation, and increases ‘T’ levels. (grade-A)



Aromatase Inhibitors for Obesity-related Male Infertility

Anastrazole 1mg 4 times a day for 3 to 6 months:

- ❑T/E ratio 5.9 to 15.6
- ❑Ejaculate vol 2.9 to 3.5 ml
- ❑Sperm conc. 5.5 to 15.6 million/ml

Raman JD, Schlegel PN. Aromatase inhibitors for male infertility. J Urol. 2002;167:624-9

AI may stimulate sperm production (grade-C)

Surgical management

- Varicocele repair?
- Vasectomy Reversal ?

Varicocelectomy

- Varicocelectomy recommended for adolescents with progressive testicular failure documented by serial clinical examination. B
- No benefit from varicocelectomy in infertile men with normal semen or in men with subclinical varicocele. A
- Varicocele repair considered in clinical varicocele with oligospermia, duration of infertility of at least 2 years and otherwise unexplained infertility in the couple. B

European association of urology 2012 guidelines

Varicocelectomy

- *Cochrane Database Systematic Review 2012:* Increase in pregnancy rates after varicocele treatment *{OR: 1.47(CI: 1.05 to 2.05)}*

- *European association of Urology guidelines 2012:* Infertile males with impaired semen and clinical varicocele and no other cause of infertility may benefit from varicocele repair.

Vasectomy reversal

Most cost-effective approach to post-vasectomy infertility. Pregnancy readily achievable after successful reversal.

Recommendation:

- Vasectomy reversal - low-risk & cost- effective method of restoring fertility B
- Sperm aspiration with ICSI second-line option for cases with failed vaso-vasostomy B

European association of urology 2012 guidelines

Assisted Reproductive Technique (ART)

Intra Uterine Insemination (IUI)

In Vitro fertilization and Intra-Cytoplasmic -Sperm Injection (IVF-ICSI)

Intra uterine insemination (IUI)

Indication of IUI:

Mild –Mod OAT's
(Motility ≥ 30%, TMSC > 10 mil/ml, Morphology ≥4%)

Antisperm antibodies

Ejaculatory dysfunct

High viscosity semen

Retrograde ejaculated semen

7 RCT: **IUI versus TI both in natural cycles:** significant difference between pregnancy rates per woman (OR 5.3)

IUI + OH versus IUI alone: no statistical difference between PR per couple for (OR 1.47).

IUI versus TI in stimulated cycles: no evidence of statistical difference in pregnancy rates per couple (OR 1.67).

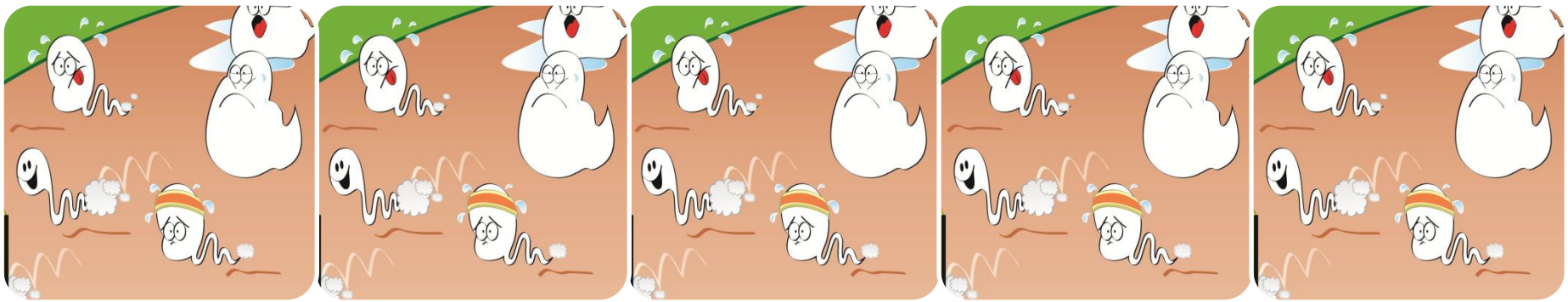
Jan 21, 2009 (up to date: August 22, 2007)

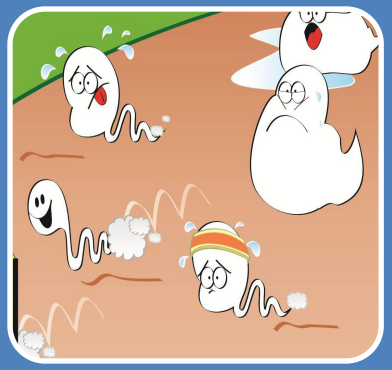
In Vitro Fertilization with ICSI

IVF-ICSI is the ultimate treatment for male infertility

- ❑Severe oligospermia (motile sperms is ≤ 1million/ml
- ❑Surgically retrieved sperms
- ❑Total immotile sperms
- ❑Globozoospermia
- ❑3-6 cycles failed IUI for mild-moderate OATs
- ❑Failed fertilization IVF

Donor insemination for every case of male infertility with no access to medical, surgical or ART treatment or genetic disorder or fear of transmission of untreatable disease





OATS

- Mild =Empirical or specific medical Rx/ IUI
- Moderate =IUI/IVF-ICSI
- Severe = IVF-ICSI

Azospermia

- Hypo hypo = gonadotropins with TI/IUI/IVF-ICSI
- Obstructive — TESA/PESA /TESE- IVF ICSI
- Testicular faiure

Miscellaneous

- Low volume / Retrograde ejaculation= IUI/ IVF-ICSI
- High viscosity = IUI/IVF-ICSI
- Globozoospermia = IVF-ICSI

Thankyou

and

best wishes for a bright new year ahead

Abha majumdar

Antioxidants for male subfertility (Review)

Showell MG, Brown J, Yazdani A, Stankiewicz MT, Hart RJ

Showell MG *et al.* Antioxidants for male subfertility. Cochrane Database Syst Rev 2011 Jan 19;(1):CD007411.

Varicocele repair vs IVF-ICSI

Varicocele repair

- Multiple chances
- Upto 70% chance of spontaneous pregnancy
- Cost effectiveness
- Natural mode
- Permanent cure
- If fails – IVF ICSI
- NOA : varicocele repair before IVF-ICSI to avoid surgical sperm retrieval
- Minimal surgical risk

IVF-ICSI

- One time chance
- 35-45% pregnancy rate per cycle
- Cost 3 x
- Artificial mode of conception
- Concerns of epigenetic disorders & congenital abnormalities of offspring
- First option if associated female factor or severe OATS
- Risk of multiple gestation & OHSS

Vasectomy reversal vs IVF-ICSI

Vasectomy reversal	IVF-ICSI
• Multiple chances • 30-70% chance of spontaneous pregnancy • Cost effectiveness • Natural mode • Permanent cure • If fails – IVF ICSI • Minimal surgical risk	• One time chance • 35-45% P/R per cycle • Cost 3 times • Artificial conception • Concerns of epigenetic disorders & congenital abnormalities of offspring • First option if female factor • Multiple gestation & OHSS