

# MEDICAL TREATMENT OF MALE INFERTILITY

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# TREATMENT

- Surgical

- Non surgical

specific therapy

nonspecific therapy

# NON SURGICAL

- ◉ Once the etiology has been identified and surgical treatment has been ruled out
- ◉ nonsurgical problems usually fall into either pretesticular or intratesticular causes

# MEDICATIONS RESPONSIBLE FOR MALE-FACTOR INFERTILITY

- Cimetidin
- Ca channel blockers
- Spironolactone
- Androgen Excess

# ILLICIT DRUGS, ALCOHOL, AND TOBACCO

- Marijuana

HPG axis, decrease serum testosterone,

spermatotoxic effect

cannabinoid Receptors, sperm motility, the acrosome reaction, mitochondrial activity

# ALCOHOLISM

hepatotoxic-induced estrogenic effects including:

- ⦿ depressed libido, and erectile dysfunction
- ⦿ inhibits male fertility

Vit C

motility



count

morphology



# INFECTIONS

- ◉ Chlamydia trachomatis
- ◉ Most common STD
- ◉ Asymptomatic 50%
- ◉ Enter sperm head count motility
  
- ◉ Azithromycin Minocycline Doxycycline
  
- ◉ Pyospemia
- ◉ Active urethral symptoms
- ◉ Unexplained asthenospermia

# UREAPLASMA UREALYTICUM

- ⦿ Lower seminal PH
- ⦿ Lower viscosity
- ⦿ Count

# ANTISPERM ANTIBODY

- ◉ 10% of male infertility
- ◉ serum and seminal plasma sperm surface
- ◉ Immobilization- agglutination of spermatozoa  
-sperm-egg interaction
- ◉ Oral corticoids
- ◉ ICSI is considered to be the treatment of choice
- ◉ antisperm antibodies and earlier failed fertilization during IVF or ICSI

# HYPOGONADOTROPIC HYPOGONADISM

- HCG 2000-5000IU 1- 3/week 6m
- hMG 75IU 3/week 12m
- FSH 100-150 IU
  
- GnRH 5-20 $\mu$ g /2 hour SQ 4m
  
- rare infertile male with HH may benefit from clomiphene

# HYPOGONADOTROPIC HYPOGONADISM

- Therapy initiated with 2000-5000 IU of hCG administered subcutaneously three times per week for six months
- FSH therapy: hMG, at 75 units SQ three times weekly
- Testis size
- GnRH pulse: 5-20  $\mu\text{g}$  every two hours

# CLOMIPHENE CITRATE

- ◉ stimulates secretion of gonadotropin-releasing hormone (GnRH)
- ◉ release of gonadotropins from the anterior pituitary.
- ◉ Increasing levels of intratesticular testosterone

# NONOBSTRUCTIVE AZOOSPERMIA

- ⦿ biopsy : maturation arrest & hypospermatogenesis
- ⦿ dosing of 25-75 mg
- ⦿ 3-9 months
- ⦿ 64.3% of men demonstrated sperm in their ejaculate with a mean density of 3.8 million/mL
- ⦿ Positive TESE
- ⦿ a well-tolerated, relatively inexpensive oral medication.

# HYPERPROLACTINEMIA

- ⦿ GT
- ⦿ LH receptor in leydig cell
- ⦿ Microadenoma <1cm 50 $\mu$ g /L
- ⦿ Cabergoline 0.5 mg /week 2mg/week 6m
- ⦿ Bromocriptine

# THYROID DYSFUNCTION

- ◉ Hypo > hyper
- ◉ Hypo: semen volume & motility
- ◉ Hyper: count & motility > morphology

# CONGENITAL ADRENAL HYPERPLASIA

- ⊙ 21 hydroxylase
- ⊙ Cortisone synthesis
- ⊙ ACTH
- ⊙ Androgen excess
- ⊙ GT
- ⊙ Treatment : glucocorticoid + clomiphen

# SPERM DNA DAMAGE MECHANISMS

- *First, DNA damage could be the result of increasing apoptosis during spermatogenesis*
- *Second, DNA breaks could be induced by chromatin remodelling during the process of spermiogenesis*
- *Third oxygen radicals could lead to sperm DNA fragmentation during transport through the seminiferous tubules and the epididymis*
- *Fourth endogenous caspases and endonucleases could cause DNA damage*
- *Fifth, exogenous factors, such as radiotherapy, chemotherapy and environmental toxicants*

# DNA FRAGMENTATION

- ◉ 75-150 IU of recombinant human FSH, given three times a week for at least 3 months
- ◉ improves sperm DNA integrity in hypogonadotropic hypogonadism and idiopathic oligoasthenoteratozoospermia men with DFI >15 %
- ◉ Giovanni Ruvolo & Maria Carmela Roccheri
- ◉ New York 2013

# THE EFFECT OF ANTIOXIDANTS ON DFI

- ◉ DNA fragmentation >25%
- ◉ 500 mg of vitamin C, 400 mg of vitamin E, 0.20 mg of selenium, 1,000 mg of L-carnitine, 20 mg of zinc, 1,000 mg of folic acid, 10 mg of lycopene
- ◉ not improve DNA integrity
- ◉ Nine fertility centers in the United States from December 2015 to December 2018

# IMPACT OF ANTIOXIDANT TREATMENT ON DNA FRAGMENTATION INDEX

- ◉ 77 men from infertile couples, with normal testosterone, LH and FSH levels and DFI  $\geq 25\%$
  - ◉ vitamin C 30 mg, vitamin E 5 mg and vitamin B12 0.5  $\mu\text{g}$ , antioxidants (l-carnitine 750 mg, coenzyme Q10 10 mg and folic acid 100  $\mu\text{g}$ ) and zinc 5 mg and selenium 25  $\mu\text{g}$
  - ◉ DFI did not change during the 6 months of antioxidant therapy
- 
- ◉ Stenqvist Lund University, Malmo, Sweden
  - ◉ started in June 2015 and ended in August 2016

# EMPIRIC MEDICAL THERAPY

- ◉ Idiopathic male infertility 25%
- ◉ Empeirikos
- ◉ Uncorrectable cause
- ◉ Prior to firm diagnosis
- ◉ Specific treatment unavailable  
failed

# EFFICACY

- ◉ Semen variation
- ◉ Heterogeneous group (etiology & baseline infertility patient selection)
- ◉ Partner evaluation
- ◉ Dosing regimen
- ◉ Treatment period
- ◉ Follow up

# ANTIESTEROGEN THERAPY

- ◉ Negative feedback of steroid in HPG
- ◉ Clomiphene citrate 12.5-50 mg /d
- ◉ Trans > Cis
  
- ◉ FSH & LH & Testosterone rise
- ◉ Semen parameter +/- sc 70%
- ◉ Pregnancy rate 0-40%
- ◉ Follow up : SA      FSH      Testosterone /m

# CLOMIPHENE

- ⦿ Elevated GT is contraindicated
- ⦿ Side effect
  - visual disturbance
  - weight gain
  - HTN
  - gynecomastia

# TOMOXIFEN CITRATE

- ◉ Metastatic breast cancer
- ◉ Less estrogenic activity than clomiphene
  
- ◉ 20 mg/ d / 6-11m
  
- ◉ SC > motility & morphology
- ◉ Pregnancy rate 20% -
  
- ◉ NL base line gonadotropin
- ◉ One week stimulation test: 40mg test  
FSH cte                      SC 50% rise

# AROMATASE INHIBITOR

- Metastatic breast cancer
- Testosterone T/E GT Estradiol
- T/E <10
- Obese man
  
- Testolactone 100-200 mg /d
- Anastrozole 1mg/d
  
- SC 80% motility NL morph
- Pregnancy rate 30%

# GONADOTROPINS

- ◉ Sub fertile men :NL or elevated gonadotropins
- ◉ Defective or inefficient bioactive FSH & LH
- ◉ Idiopathic oligospermia or NOA
  - HCG 5000IU 2-3/week 4m SA60% PR35%
  - hMG 75IU 2-3/week 1-3m SA19% PR15%
- ◉ Anabolic 3m wait
  - HCG10000IU 2/w +/- hMG 75IU/d
- ◉ IVF failure FSH 150IU 3/w 3m

# GNRH

- ◉ Idiopathic oligospermia      mod> severe
- ◉ Intranasal    SQ    pump
- ◉ Semen parameters 67%
- ◉ Pregnancy rate 24%

# ANDROGENS

- ◉ Testosterone is 50 fold of serum
- ◉ Epididymal function
- ◉ Low dose T easily metabolised by liver
- ◉ Extraordinary high dose of animal model
- ◉ Floxymesterone 20mg/d 6w

# TESTOSTERONE REBOUND THERAPY

- ⦿ High dose testosterone for pituitary inhibition
- ⦿ Withdrawal for rebound testosterone
- ⦿ Oligospermia    semen parameter 20-67%  
pregnancy rate 14-41%
- ⦿ Azoo
- ⦿ Chemotherapeutic agent

# KALLIKEREIN

- ◉ Polypeptide enzyme
- ◉ Source : pancreas
- ◉ Oral & parenteral
- ◉ Regulation & stimulation of sperm motility
- ◉ 600 KU/d
- ◉ Semen parameter & pregnancy rate +/-
- ◉ Inflammation of epididyme & prostate

# INDOMETHACIN

- PG steroidogenesis & spermatogenesis  
sperm motility
- 75 mg/d
- Oligospermia
- Pyospermia
- ASA
- FSH & LH & Testosterone
- Motility & Count
- Pregnancy rate 35%
- Gastritis

# PHOSPHODIESTERASE INHIBITOR

- Petoxyfylline 400-800mg/d
- Sildenafil
- Motility    invitro+  
                  invivo-
- CAMP
- Micro circulation

# ZINC

- ◉ Semen rich in zinc
- ◉ Prostate
- ◉ Deficiency
- ◉ High dose      detrimental sperm function
- ◉ 66mg/d

# L-CARNITINE

- ◉ intracellular energy metabolism as well as spermatozoa
- ◉ membrane stabilization
- ◉ Carnitine also has an antioxidant capacity
- ◉ Epididymal secretions
- ◉ Motility
- ◉ 1-2 g/ d

# VIT A

- Sperm maturation

- 25000IU

# VIT E

- ◉ Sperm count , motility , morphology
- ◉ Acrosome reaction
- ◉ ICSI
- ◉ 400 IU/d

# A AGONIST

- ⦿ Retrograde ejaculation
- ⦿ Emission disorder
- ⦿ Phenylpropanolamin 75mg BD
- ⦿ Psuedoephedrine 60mg QID
- ⦿ Imipramine 25mg BD

# LICOPEN

- Testis & semen
- Idiopathic OAT
- 2mg BD
- 3m

# FOLIC ACID

- ⦿ **Morphology**
- ⦿ **Motility**
- ⦿ **Count**
  
- ⦿ **5mg**
  
- ⦿ **3-6m**

# ARGININ

- ◉ Aminoacid

- ◉ Count

- ◉ Motility

# COQ10

- ◉ Antioxidant
- ◉ Sperm energy