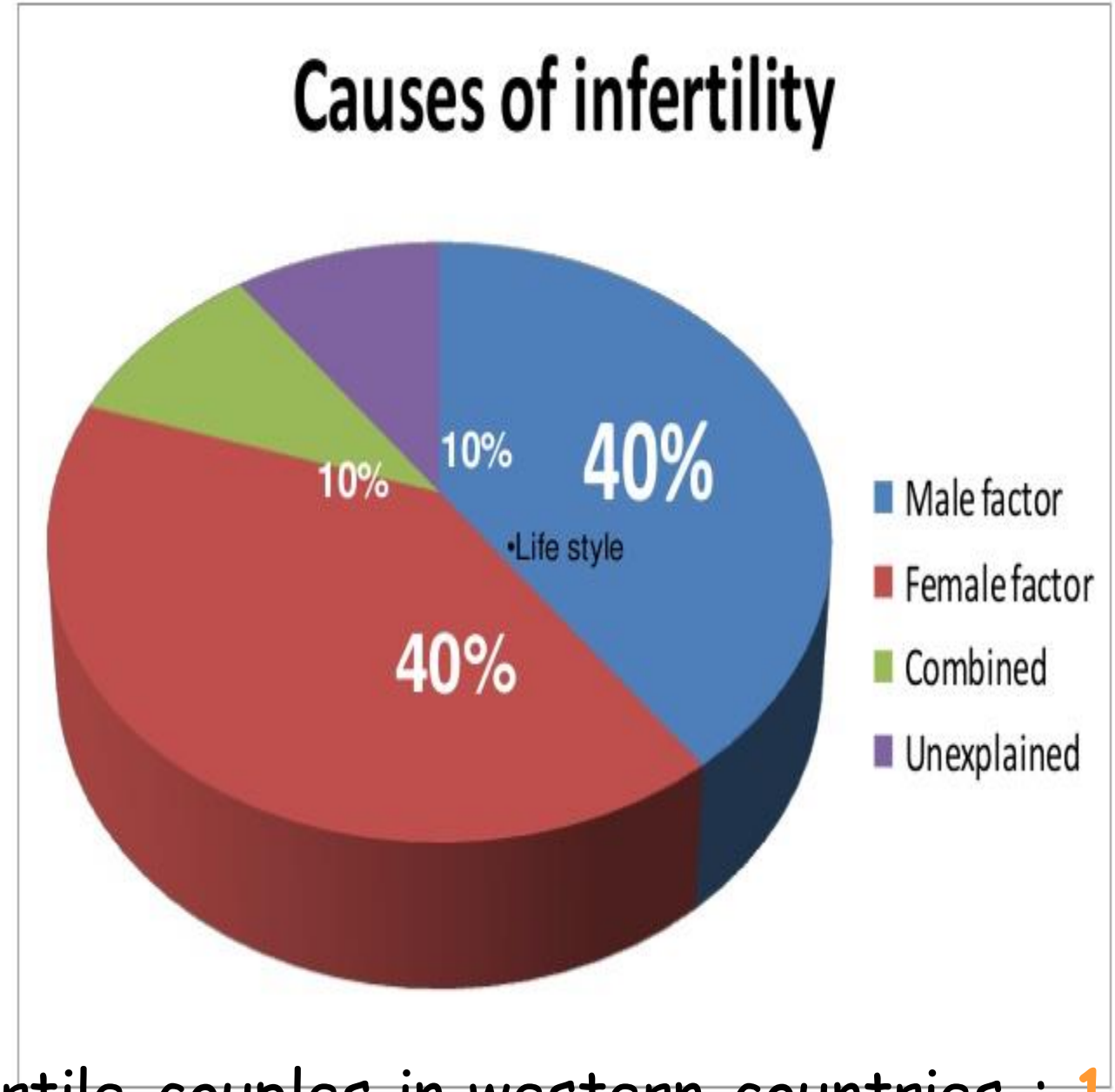
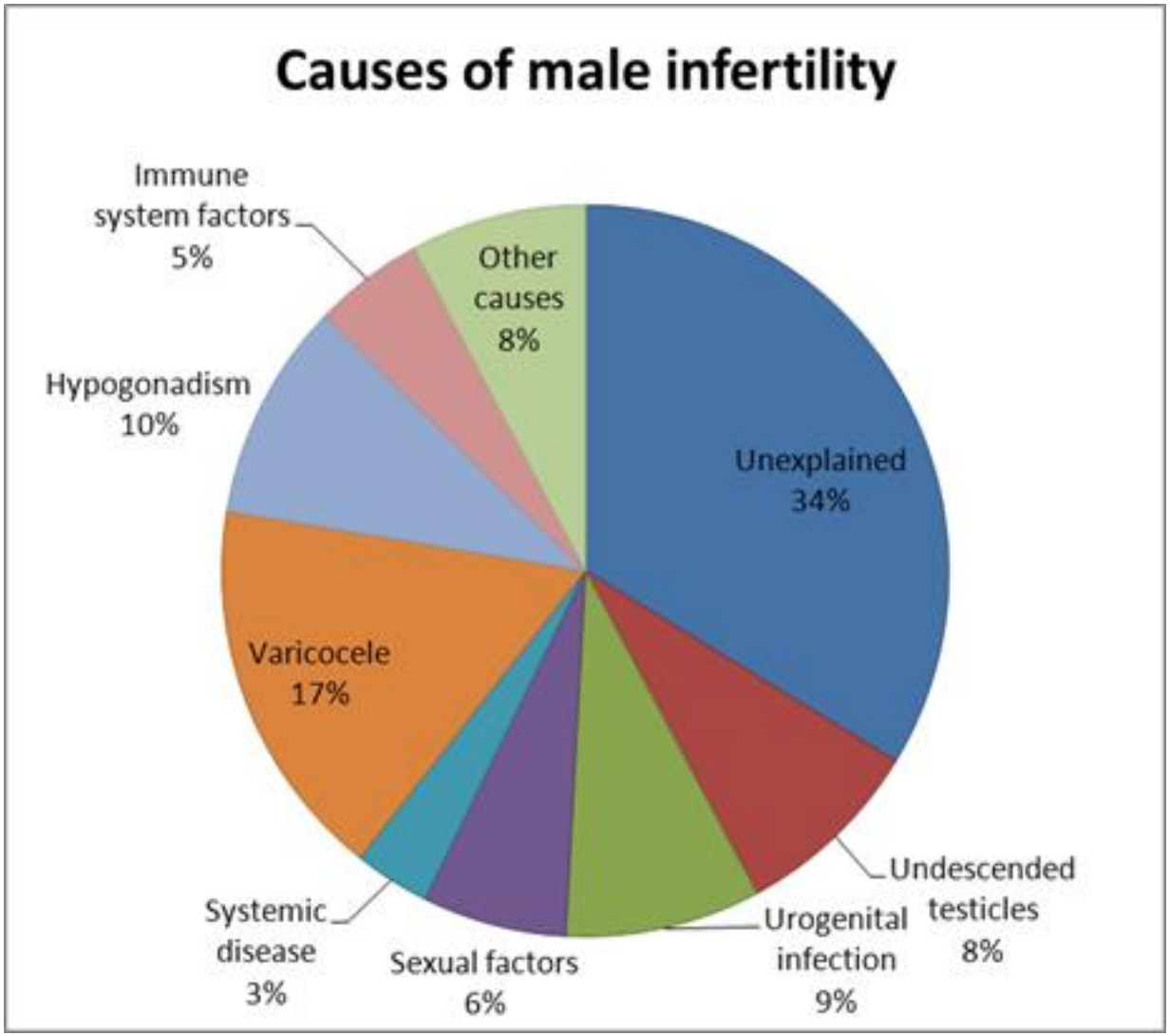
Part 2:
Medical Genetics and infertility


infertility
sperm
male
men
problems
testes
hormonal
production
ejaculation
Responsibility
testicular
causes
many
psychological
testosterone
fertility
count
infertile
impotence
Problems
abnormal
Syndrome
Klinefelter
testicles
libido
low
damage
therapy
include
hormones
FSH
like
behavioral
couples
decreased
thyroid
technique
list
problem
gland
damaged
scrotum
Torsion
found
GnRH
May
back
Also
successful
caused
following
inability
motility
available
STDs
care
insemination
spermatic
quality
analysis
replacement
LH
penis
secondary
However
pathway
stimulate
cells
lifestyle
germ
using
loss
women
million
percent
man
and/or
drug
seek
resulting
semen
sexual
cell
often
one
abdomen
masturbation
number
small
sphincter
stress
reduces
adrenal



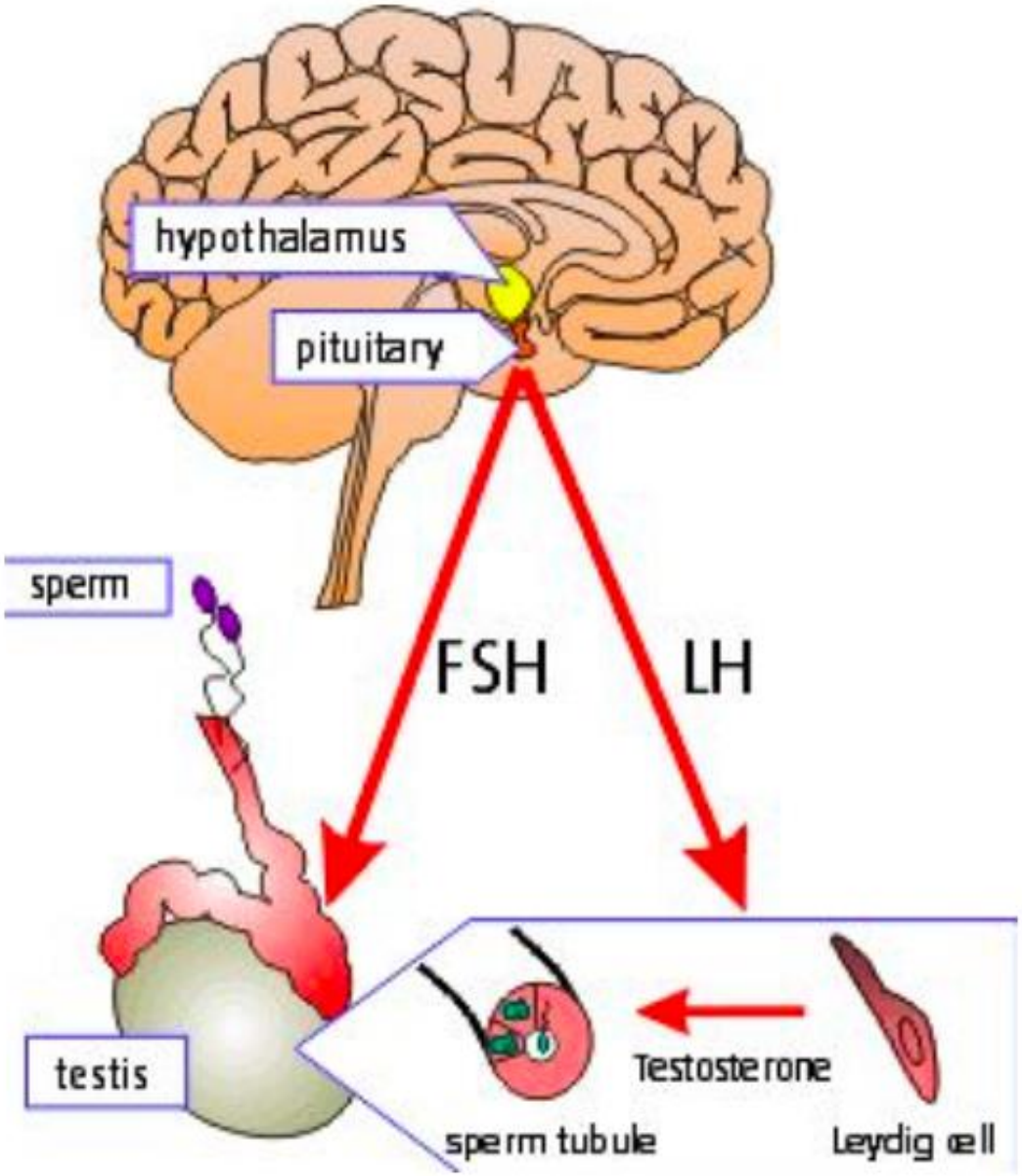
- Infertile couples in western countries : 15-20% (WHO)


Causes of male infertility
Immune system factors 5%
Other causes 8%
Hypogonadism 10%
Unexplained 34%
Varicocele 17%
Undescended testicles 8%
Urogenital infection 9%
Sexual factors 6%
Systemic disease 3%

Genetic testing in infertile males

Before to start….

- **Get infromation about:**
  - Clinical history (varicocele, criptorchidism, infective diseases, drug abuse etc.)
  - Possible exposure to environmental factors dangerous for spermatogenesis
- **To identify the best genetic test:**
  - To have a clear picture of
    - Sperm count
    - FSH, LH and Testosteron levels
  - To distinguish among:
    - pre-testicular conditions,
    - testicular conditions
    - post-testicular conditions

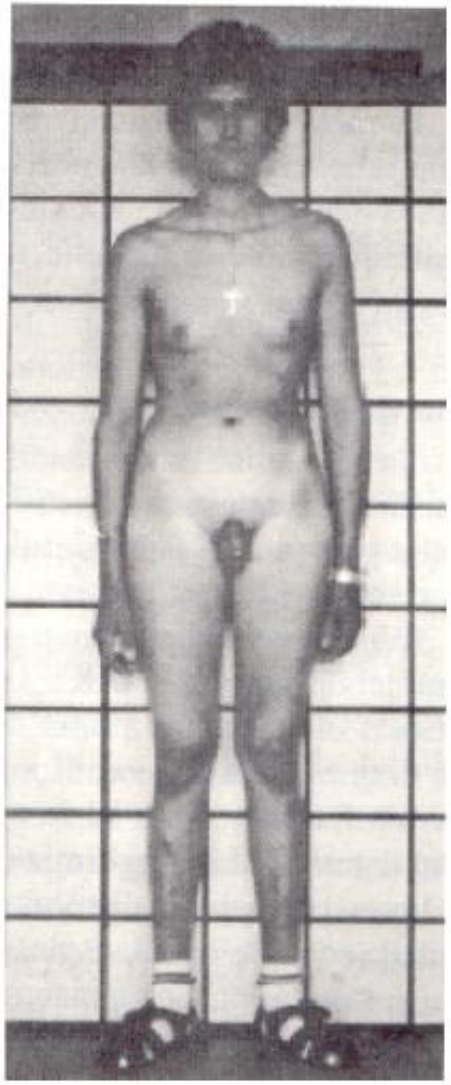

hypothalamus
pituitary
sperm
FSH
LH
testis
Testosterone
sperm tubule
Leydig cell

CAUSES

PRE TESTICULAR	TESTICULAR	POST TESTICULAR
ENDOCRINE: • Hypogonadotropic hypogonadism • Hypothyroidism • Hyperprolactinaemia • Diabetes **COITAL DISORDERS:** • Erectile dysfunction • Ejaculatory failure	**GENETIC:** • Klinefelter syndrome • Y chromosome deletion • Immotile cilia syndrome **CONGENITAL:** • Cyptorchidism • Infective • Antispermatogenic agents heat, irradiation, drugs, chemotherapy **VASCULAR :** Torsion Varicocele **IMMUNOLOGICAL**	**OBSTRUCTIVE:** **Epdidymal** congenital infective **Vasal** Genetic: cystic fibrosis. Accquired: Vasectomy Ejaculatory duct obstruction Accessory gland infection Immunological Idiopathic post vasectomy

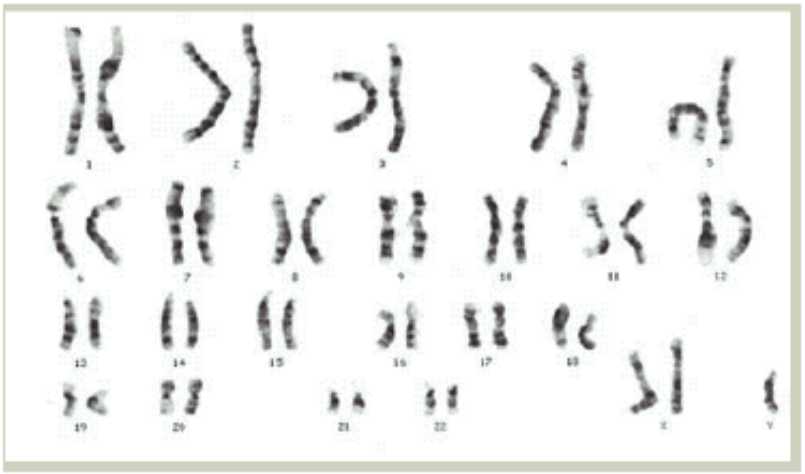
Klinefelter syndrome (47,XXY)

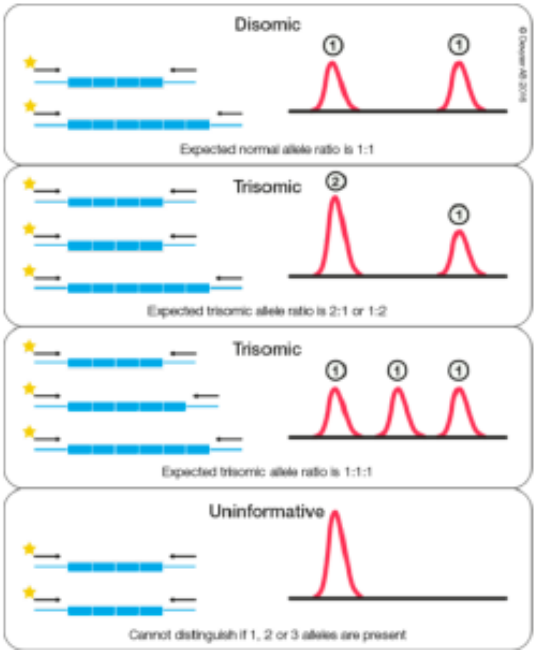
- Prevalence: 1:500 – 1:1000 males
- Karyotype 47, XXY
- Common features:
  - Infertility
  - High stature
- Other possible features:
  - Female secondary traits



Genetic testing for KS

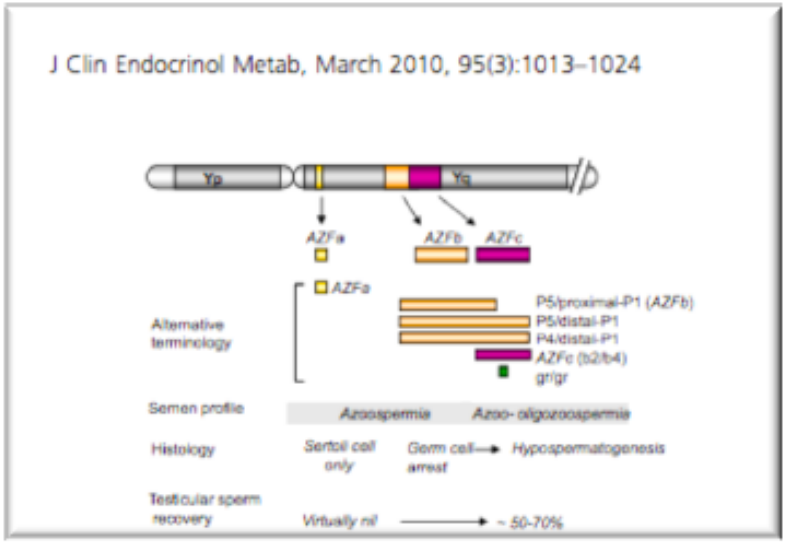
- Cytogenetic investigation
  - Count up to 100 metaphases in order to verify the presence of mosaicisms
- QF-PCR
  - When peripheral blood lymphocytes are not available





Non obstrucive azoospermia or severe oligozoospermia (<5ML/ml) (2)

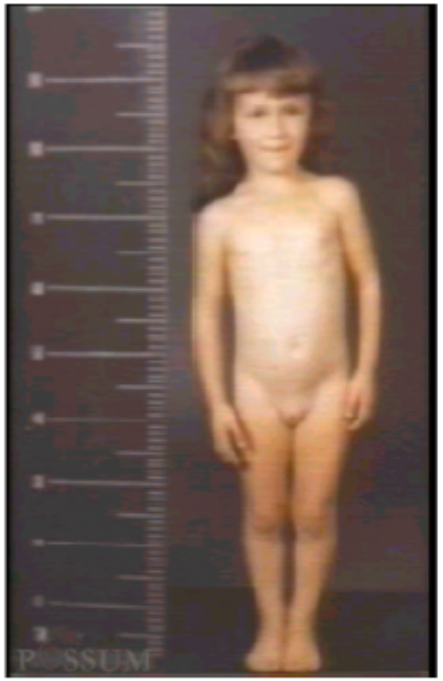
- **Microdeletions of the Y chromosome**
  - 10% of cases , 1/2500 in general population
  - To search only after cytogenetic investigation
  - Detection rate in not selected patients <2%



Genetic testing in female infertility

Premature Ovarian Insufficiency (1)

- **Karyotype:**
  - 13% of cases carriers of numeric or structural aberrations of the X chromosome
  - Most frequent: 45,X karyotype (Turner syndrome)
    - 40% of cases mosaic 45,X/46,XX (POI)
    - Count up to 30-50 metaphases
  - Structural abnormalities
    - Xq Isochromosome
    - Xq deletions or translocations
      - Xq26-Xqter (POF1), Xq13.3-Xq21.1 (POF2)
    - Xp deletions or translocations
      - Xp11.1-Xp21



Premature Ovarian Insufficiency (2)

- **Search for premutations of the FMR1 gene:**
  - Association with POI:
    - 3% of sporadic cases
    - 15% od familiar cases
  - Prevalence of POI in women with FMR1 premutation:
    - 13-26%
- Technical gold standard: High Resolution Methylation PCR