genetics

meiosis & mitosis
(some imp.facts)

- ovum is largest cell in human body (120-140micron)
- crossing over during meiosis varies according to the type of chromosomes.

cells that **donot** divide after birth are:

- neurons except olfactory neurons.
- muscle cells.

in oogenesis a primary oocyte give rise to one haploid ovum & three polar bodies.

- while in spermatogenesis a primary spermatocyte give rise to 4 spermatids & ultimately four functional spermatozoa.

Meiosis results in-

- reduction of no. of chromosomes to haploid in daughter cells.
- recombination of genetic materials
- random assortment of chromosomes(mendel's 3rd law)
- This ultimately give rise to haploid no. of cells with a variant composition from parents which is responsible for genetic diversity in human species.

- colchicine is drug which arrest mitosis of cells in metaphase ,thus added to cell cultures during preperation for study of chromosomes.
- **apoptosis** is programmed death of a cell.this is genetically decided by cell.there is activation of intracellular enzymes and degranulation of lysosomes leading to degeneration of cell components & its death.e.g **cyclical breakdown of endometrium of uterus causing mensturation, removal of old cells of intestinal epithelium.**

Chromosomes

- they are vehicle of inheritance which facilitate reproduction & maintainance of species.
- they are thread like structures in nucleus and made up of genes.
- study of chromosomes & cell division is **cytogenetics.**
- **karyotyping** is characterization of chromosomes according to their size , shape & distribution of stain taken up by them.

Chromosomal abnormalities

- numerical abnormalities
- structural abnormalities

numerical abnormalities

- alteration in chromosomal no.
- are of two types
- **aneuploidy**---occur as a result of **addition** or **loss** of one or more chromosomes , most of abberations takes place due to non-disjunction.(i.e. failure of sepertion of bivalent chromosomes during meiosis 1or a pair of chromatids during mitosis.
- E.g trisomy, monosomy, mosaicism.

- **polyploidy**—addition of one or more complete haploid set of chromosomes to the normal diploid no. of chromosomes

Trisomy

- presence of three copies of chromosomes instead of normal 2 in a cell.
- cause—due to non disjunction of a chromosome or chromatid in one of fertilizing gametes.
- Its occurence increases with age of mother.
- Trisomy 21 is commonly known as **down's syndrome** or mongolism

- cytogenetics– it usually follow fertilization of two gametes out of which one has two chromosome 21.
- Rarely it can occur due to translocation of long arm of chromosome 21 to a D and G group of chromosome.

Features ---

- mental retardation
- short stature
- brachycepaly
- Presence of epicanthal folds
- protruding tongue , small ears & flat occiput
- Flat nasal bridge
- brush field spots in eye
- All males are infertile while females have reduced fertility.

- Risk factors
- higher inccidence with advancing maternal age
- family history of down’s syndrome
- radiation injuries.

Part of a regular cell showing chromosome 18, 19, 20, and 21 pairs

Part of a Down Syndrome child's cell showing chromosome 21 pair with 1 extra chromosome

Down Syndrome

Trisomy 18

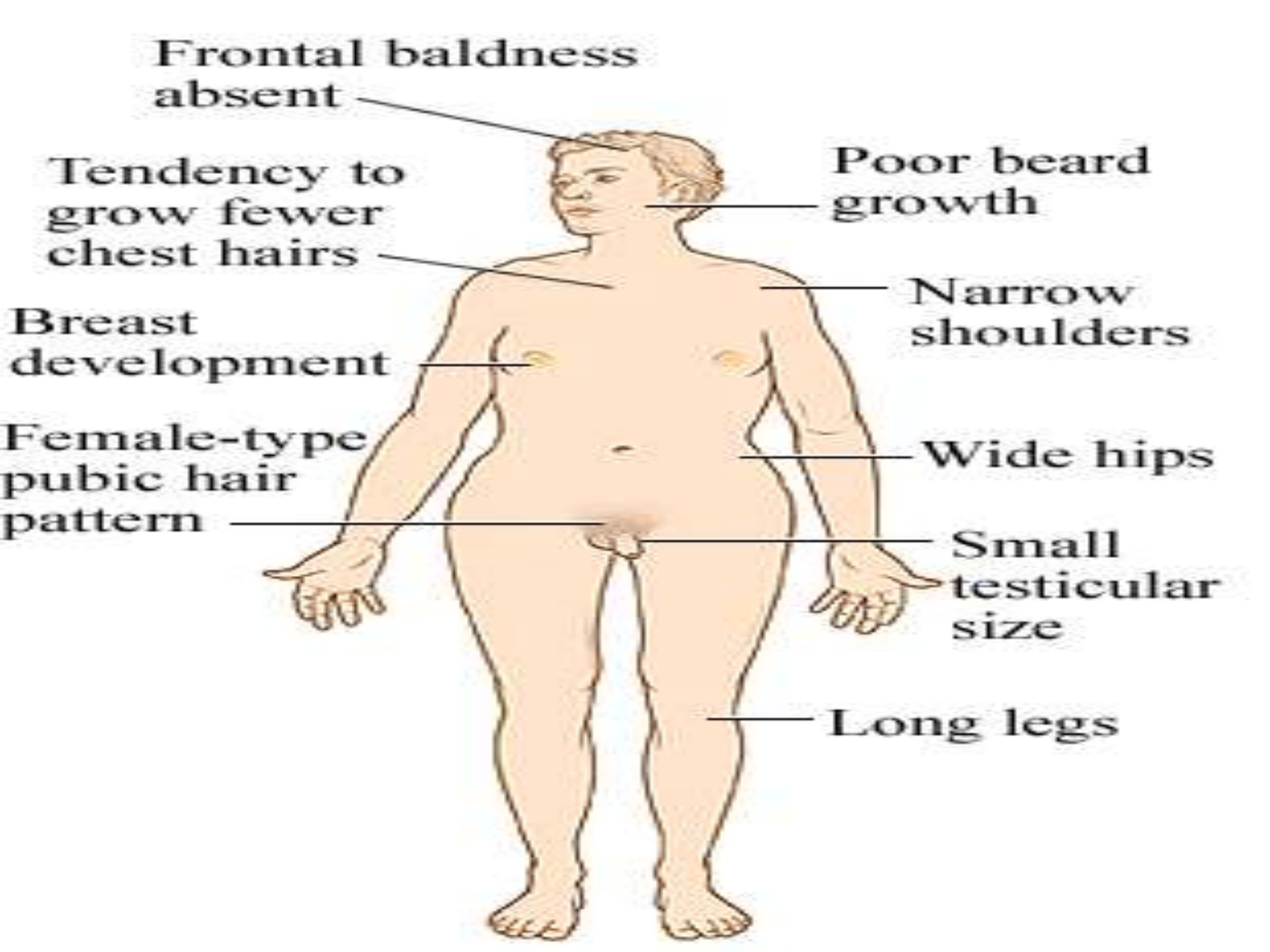
- **Edward syndrome**
- mostly these pregnancies undergo still births or spontaneous abortion
- newborn has ---small face with prominent occiput,
- Flat nose
- Low set ears
- Micrognathia
- overlapping of fingers & rocker bottom heels.

Trisomy 13

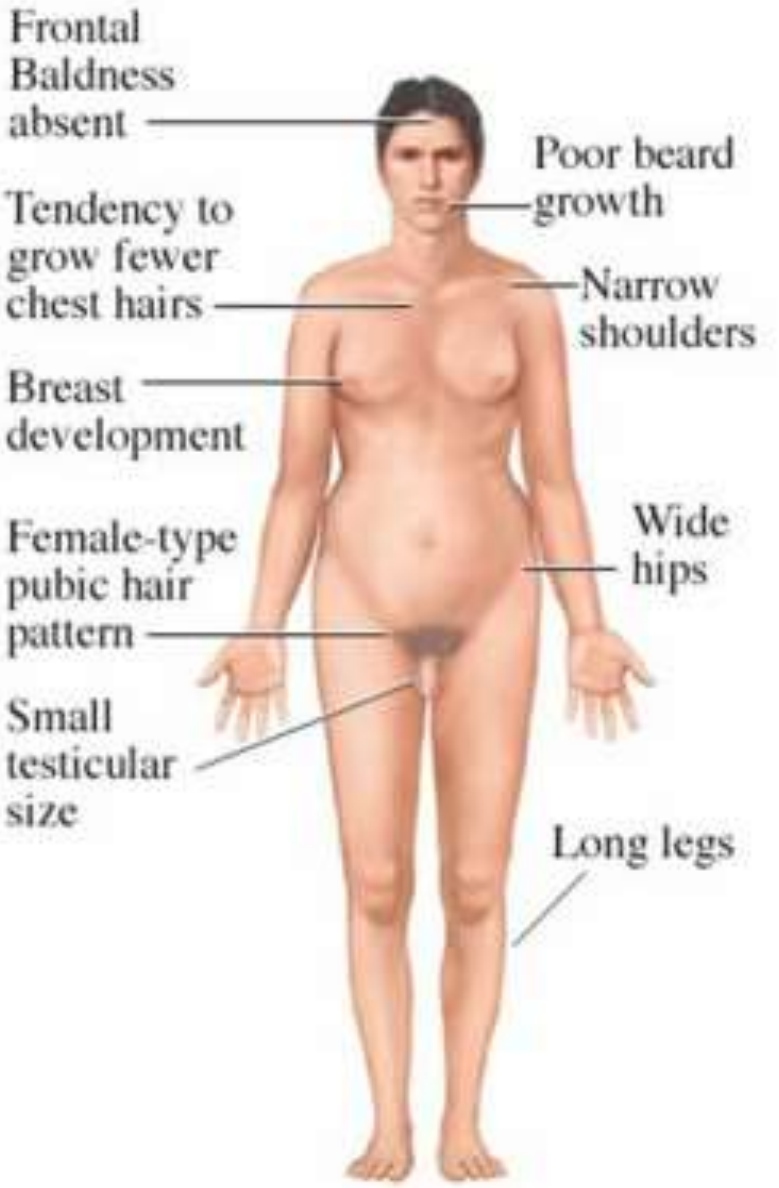
- patau’s syndrome
- less common
- newborn has CNS malformations
- cleft palate
- hairlip
- Lethal cardiac anomalies
- profound mental retardation in survivers.

Klienfelter’s syndrome

- it is trisomy of sex chromosomes(47,xxy)
- A young boy with this presents with a mild developmental delay and behavorial immaturity .
- adult male presents with– small testes ,dysgenesis of seminiferous tubules , gynecomastia & poor musculature.most males are infertile.

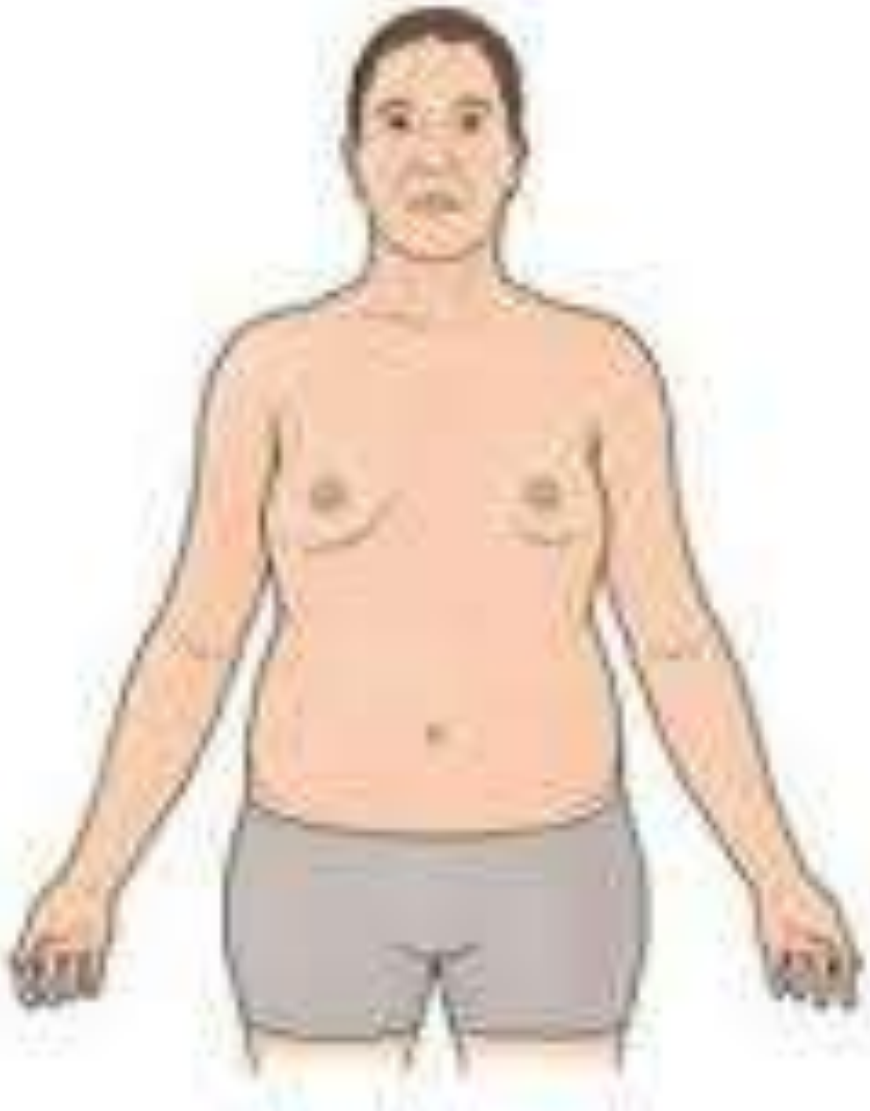

Frontal baldness absent
Tendency to grow fewer chest hairs
Breast development
Female-type pubic hair pattern
Poor beard growth
Narrow shoulders
Wide hips
Small testicular size
Long legs

Klinefelter syndrome



- Lower IQ than sibs
- Tall stature
- Poor muscle tone
- Reduced secondary sexual characteristics
- Gynaecomastia (male breasts)
- Small testes/infertility

The signs.



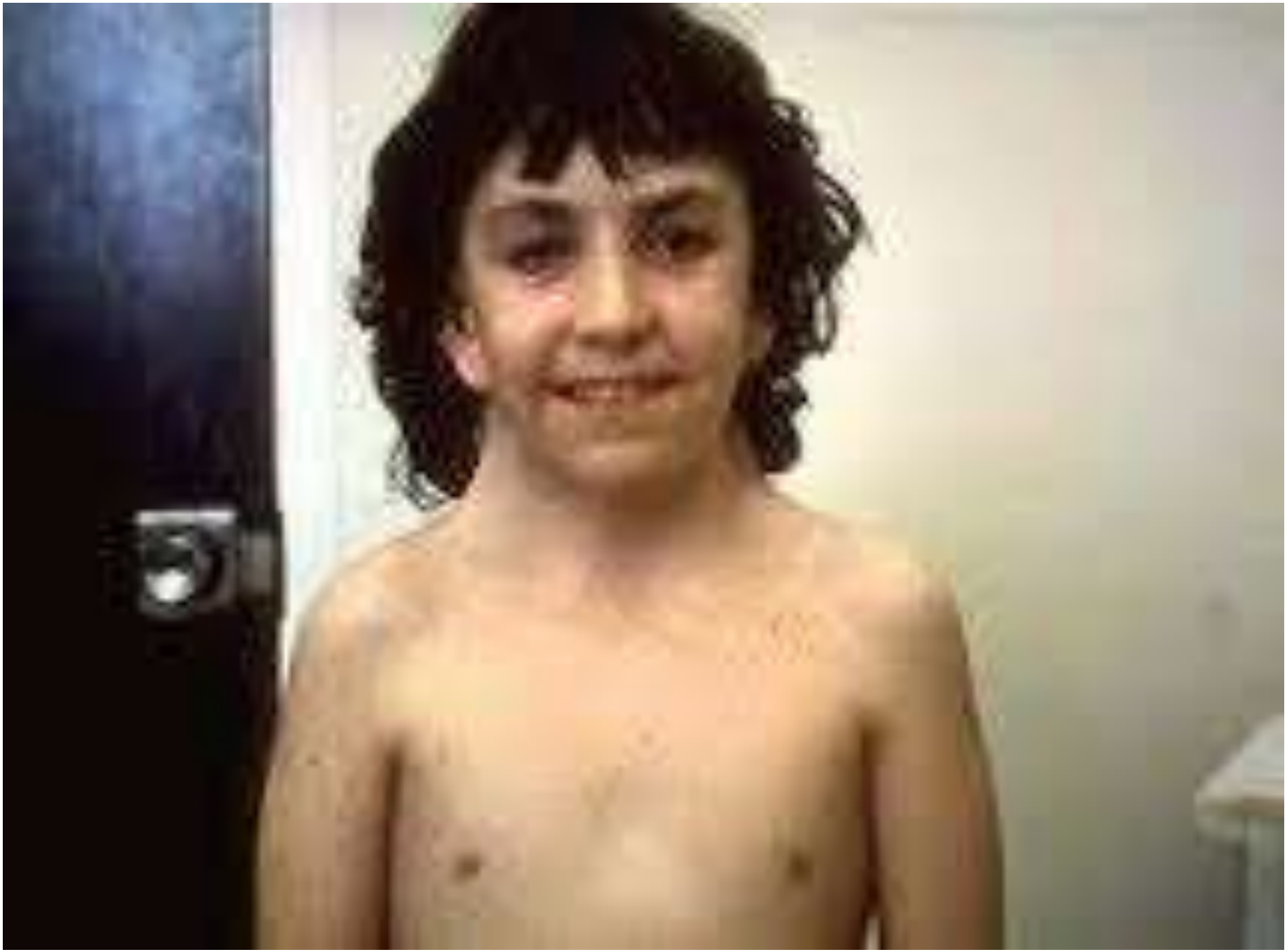
- A taller less muscular body than males there age.
- Broader hips and longer legs.
- Larger breast.
- Weaker bones.
- A lower energy level.
- Smaller penis and testicles.
- Delay in puberty or go a parcel amount.
- Less facial and body hair following puberty.

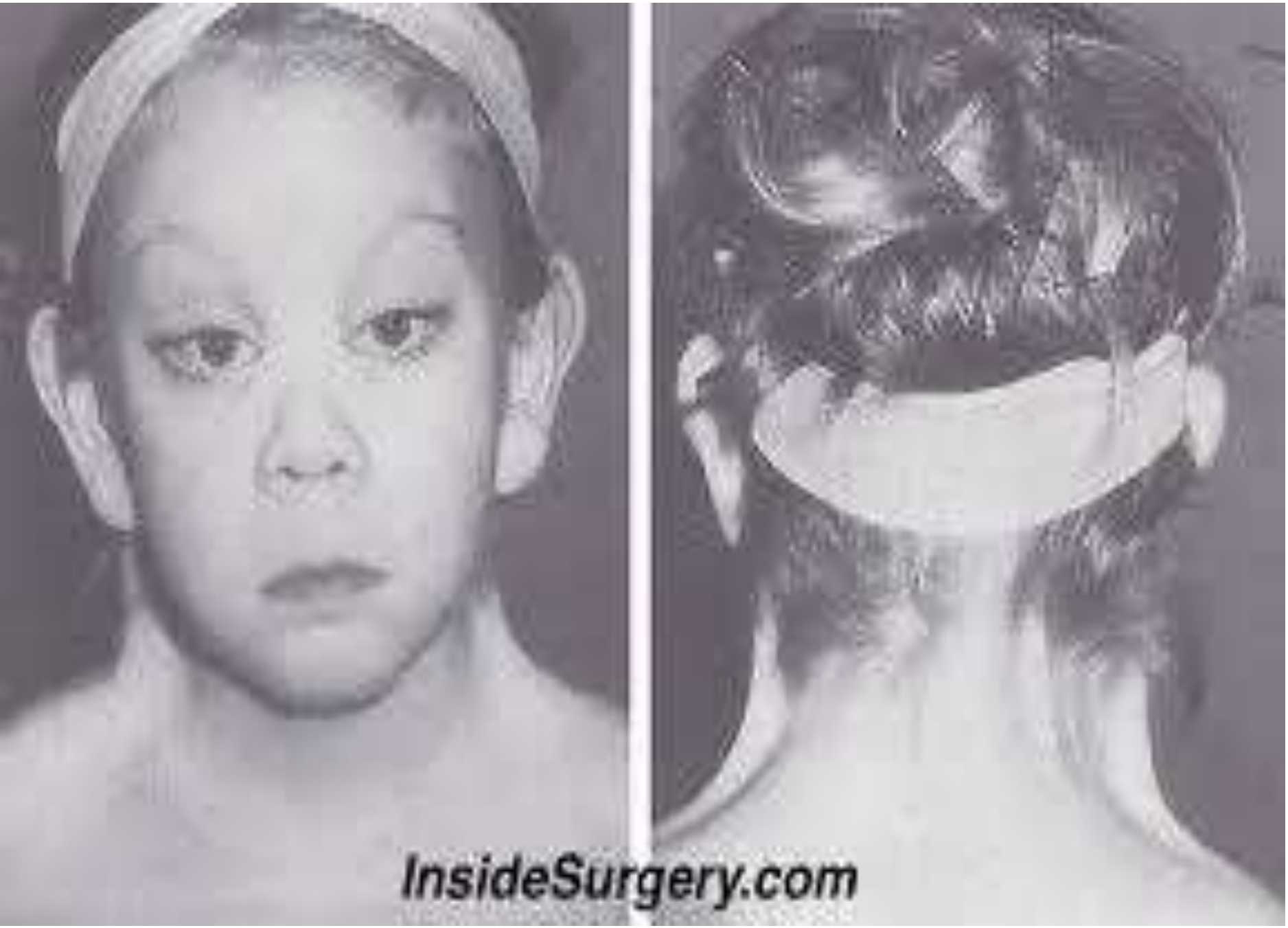
Monosomy

- characterized by presence of only one member of homologus pair of chromosomes in karyotype
- autosomal monosomies are not seen in livebirths / in early spontaneous abortions because they are fatal to conceptus.
- turner's syndrome

Turner's syndrome

- monosomy (45, X0)
- Patient is female & presents with—
- short stature
- webbing of neck
- low hair line at nape of neck
- primary or secondary amenorrohea
- streak ovaries
- majority are infertile




InsideSurgery.com

- **Causes & risk factor**
- during fertilization one of gamete lacks x-chromosome,occurs due to non-disjunction or anaphase lag during cell division in which x-chromosome is lost to non fertilizing daughter cell of original germ cell.

Structural defects in chromosomes

deletion	**Cri-du-chat/cat cry syndrome**	**Deletion of terminal portion of short arm of chromosomes** 5(5p-**).newborn presents with---**round face, hypertelorism,micrognathia,severe mental retardation, cardiac defects, cry that **resembles that of a cat.**
	Wolf-hirschhorn syndrome	Deletion of short arm of chromosome **4(4p-)features—prominat forehead & broad nasal root, short philtrum,mouth is downturned,severe mental retardation, cardiac defects, growth failure.**
microdeletion	Prader-willi syndrome	Microdeletion of long arm of **15q,** Infant presents with---**profound hypotonia Mental retardation, trunkal obesity**
Interstitial deletion	WAGR syndrome	Interstitial deletion of short arm of **11**.child presents **with—wilm's tumour, aniridia, genital abnormalities,growth retardation**.

Prenatal diagnosis

- genetic abnormalities in a conceptus can result in—
- **Spontaneous miscarriges** (mostly first trimester)
- **gross congenital abnormalities** in newborn -2-3% newborns have atleast one congenital amnormality , that leads to high perinatal morbidity & mortality.
- **abnormality** in childhood & adult life e.g blindness, deafness malignancies.

Indications of prenatal diagnosis

- advanced maternal age at conception (>35yrs)
- previous history of genetically abnormal child or child with gross congenital anomly
- multiple miscarriges
- Family history of genetic disorder
- Consanguinous couples
- preimplantaion diagnosis in cases of in-vitro fertilization.

Preimplantaion diagnostic procedures

non-invasive tests—pedigree chart to be made with history

- **ultrasound** for looking structural anomalies **(done at 16-22 wks)**.
- invasive tests—
- Amniocentesis—usg guided amniotic fluid aspiration(16-18 wks), or at 10-14 wks for early diagnosis. Cells obtained are cultured for genetic analysis and takes 2-3 wks

- **chorionic villus sampling(CVS)enables** prenatal diagnosis during first trimester.

fetal loss is higher 1-2%,requires experienced operator ,can be obtained transcervical /transabdominal.

percutaneous usg guided fetal blood sampling/ cordocentesis—useful in assesment of fetal hemogram , fetal injection & provide high quality karyotype.

- Involves aspiration of fetal blood from cord near its insertion in placenta.(done in 18-20 wks)

- **fetoscopy**

Visualisation of fetus by endoscope

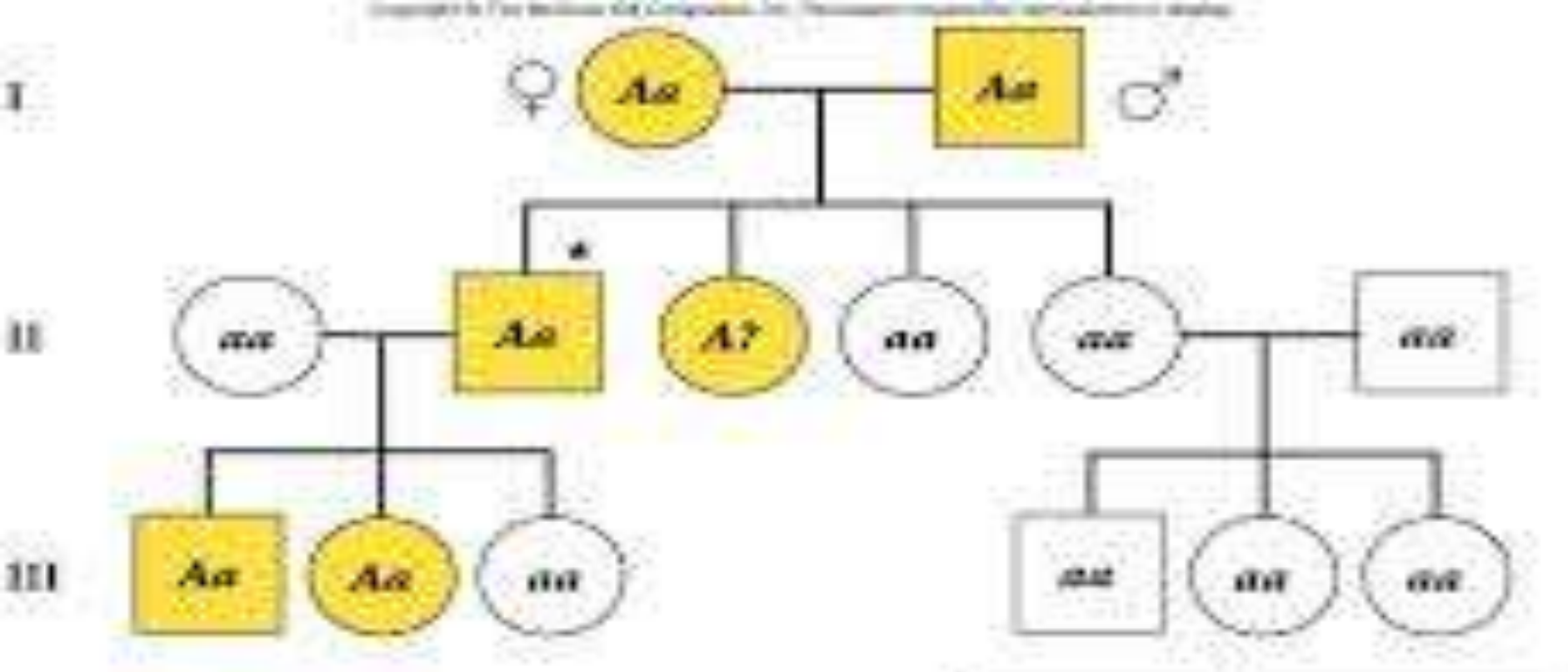
- **percutaneous usg guided fetal skin biopsy-**--- perfirmed at 18-20 weeks of gestation to detect skin abnormalities.

Methods to detect early genetic abnormality

- **karyotyping**
- ***FISH***(flouroscent in situ hybridisation)
- **flow cytometry**

methods to detect DNA & RNA---

- **southern blot** technique—detect DNA
- **northern blot** technique—detect RNA
- **western blot** tecnique—to identify size & amount of abnormal proteins present in sample,it makes use of antisera specific for proteins.

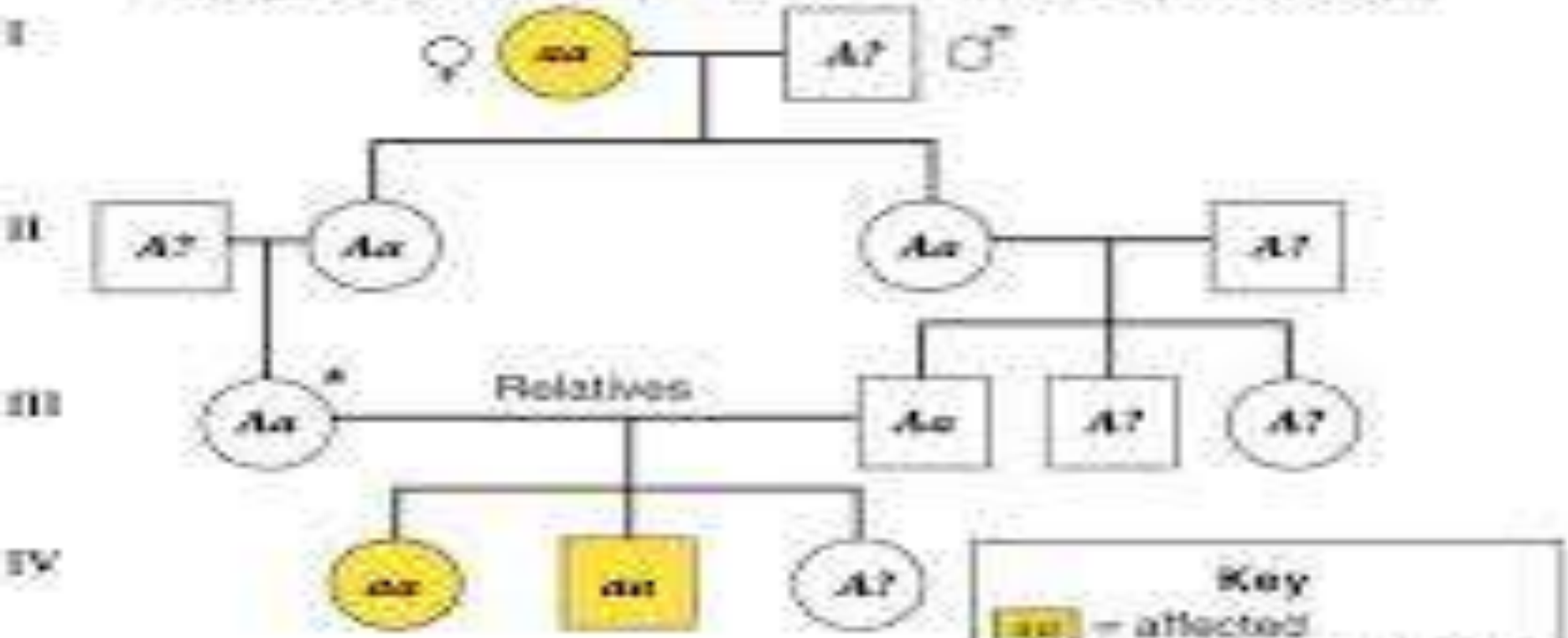


Autosomal dominant disorders

- Affected children will usually have an affected parent.
- Heterozygotes (Aa) are affected
- Two affected parents can produce an unaffected unaffected child.
- Two unaffected parents will not have affected children.
- Both males and females are affected with equal frequency.

Autosomal dominant

- occurs due to mutation in a dominat gene on an autosome leading to particular trait ,
- trait is transmitted from one generation to other equally to male or female offsprings (vertical transmission)
- risk of transmission of disorder is 50% if one of parent has dominant trait.
- unaffected family member do not transmit disorder.E.G retinitis pigmentosa , neurofibromatosis 1, huntington disease.

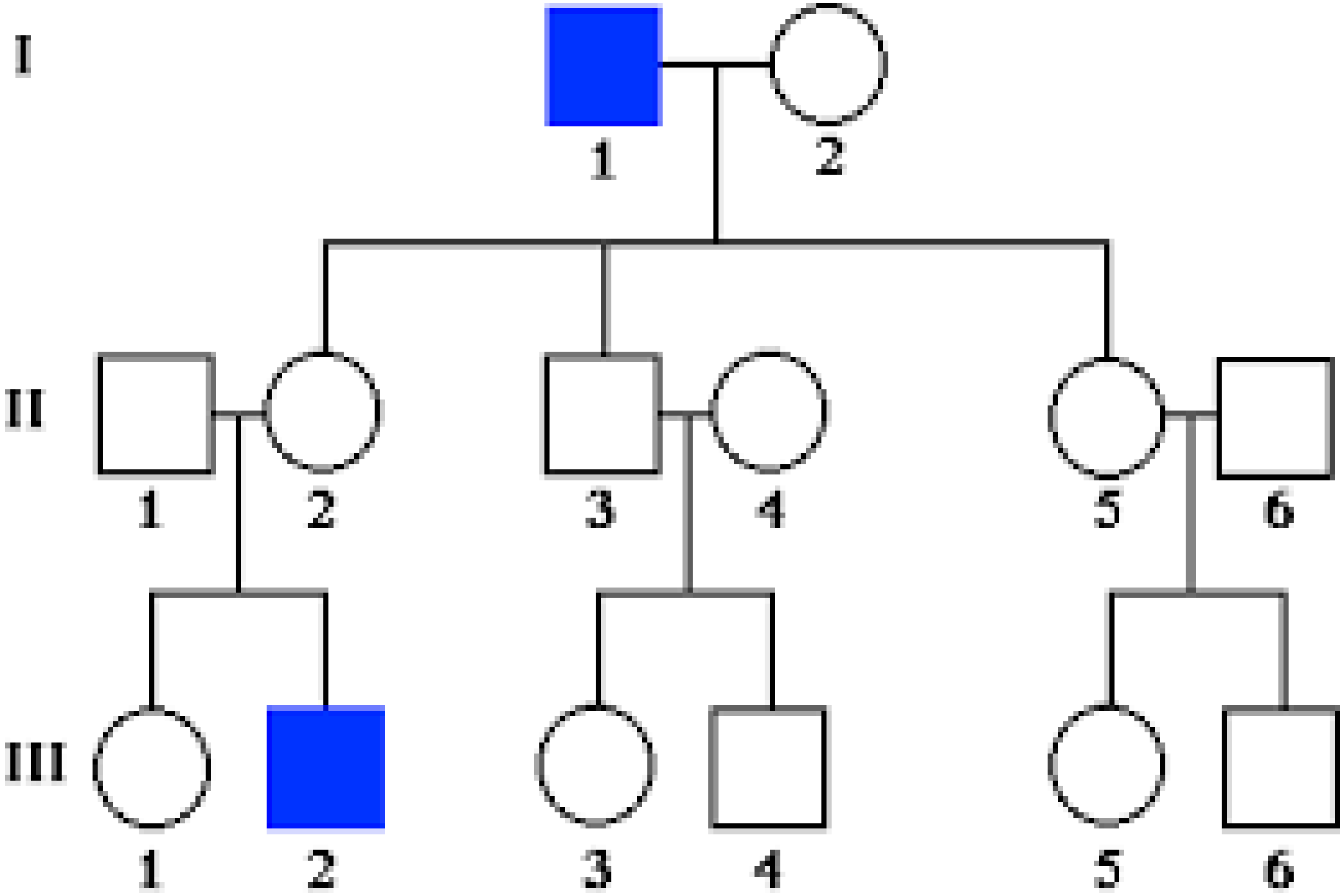


Autosomal recessive disorders

- Most affected children have unaffected parents.
- Heterozygotes (Aa) have an unaffected phenotype.
- Two affected parents will always have affected children.
- Affected individuals with homozygous unaffected mates will have unaffected children.
- Close relatives who reproduce are more likely to have affected children.
- Both males and females are affected with equal frequency.

Autosomal recessive

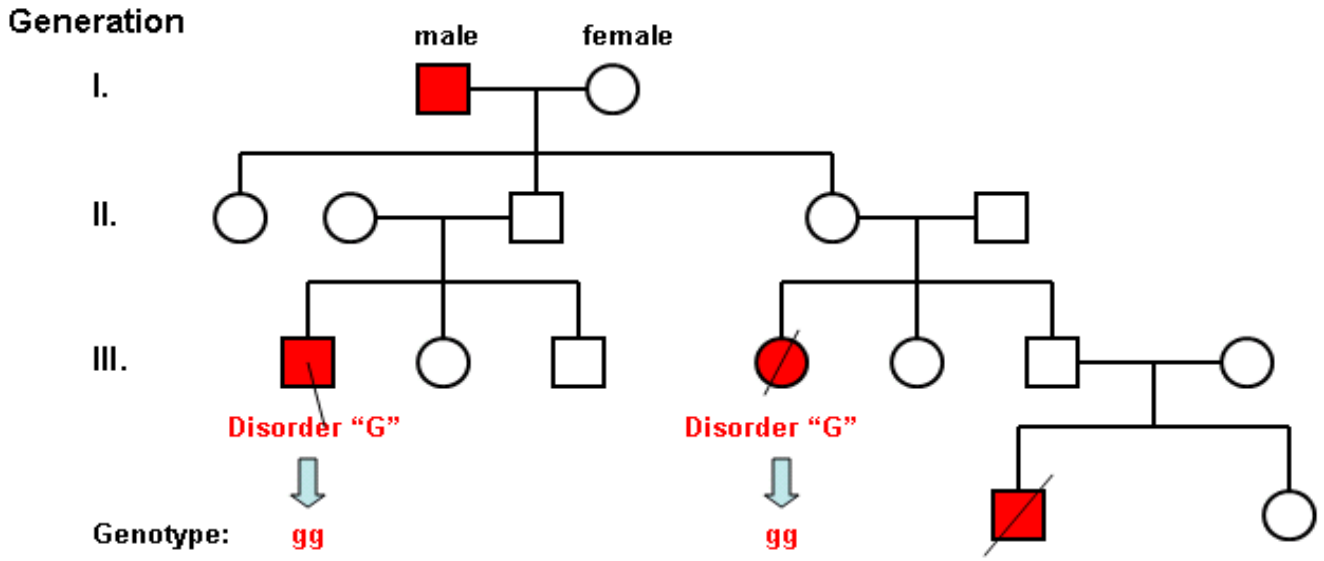
- Mutated gene is expressed only in a homozygous state ,
- affected individual's are usually siblings (horizontal transmission),with equal distribution in males & females.
- successive generations may skip having disorder till two carrier partner's meet .
- parents of affected individual are apparently healthy as they are hetrozygotes.e.g taysach's disease ,cystic fibrosis, sickle cell anemia.



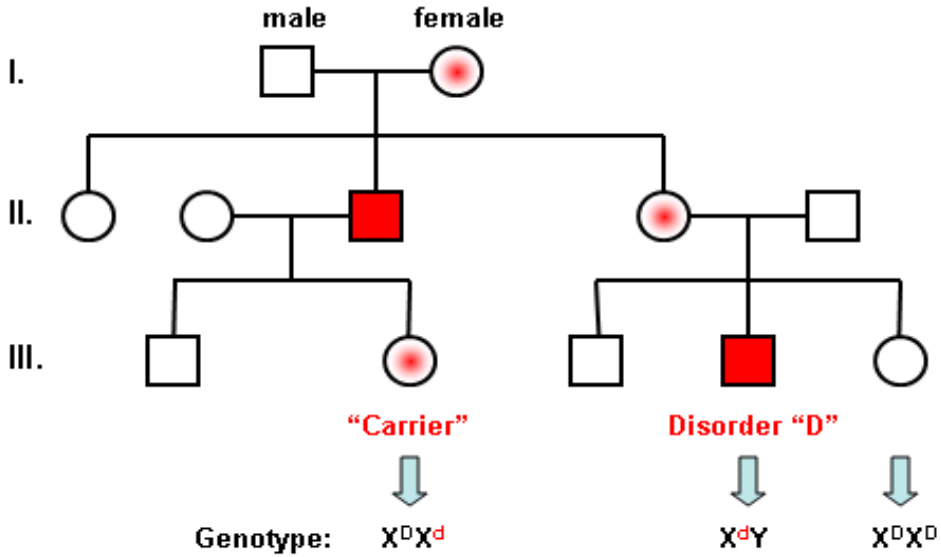
Pedigree 7. X-linked recessive inheritance

Overview: Pedigree Analysis in Genetics

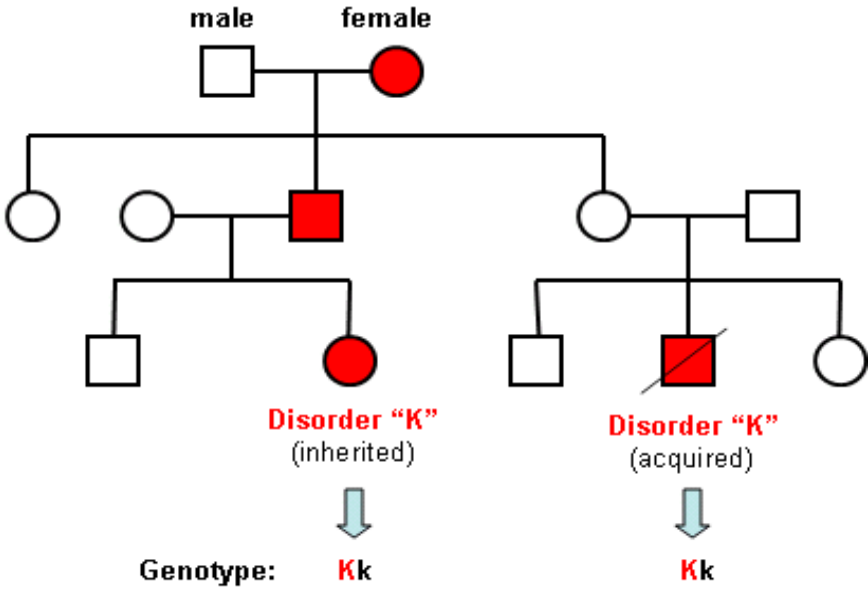
I. Autosomal recessive trait



III. X-linked inherited trait



II. Autosomal dominant trait



X-linked recessive trait

- most common form of sex-linked abnormalities,
- disorder affects only males , while females are unaffected in families
- disorder is transmitted by carrier females to their sons,
- affected males , can transmit the disorder to their grandchildren via obligate carrier daughters.e.g icthyosis, G6PD, red & gree colour blindness, duchene muscular dystrophy.hemophillia.