GENETICS

GENETIC COUNSELING (SE)

- It is a process of communication and education relating to the development of transmission of a hereditary disorder.
- An individual who seeks genetic counseling is called consultand and person who gives counseling is called counselor.
- Genetic counselors should be expert educators, skilled in translating the complex language of genomic medicine into terms that are easy to understand.
- Genetic counselors provide information and support to families who have members with birth defects or genetic disorders, and to families who may be at risk for a variety of inherited conditions.

The steps in genetic counseling are-

- diagnosis,
- risk assessment,
- discussion of options,
- long term contact and support
- prognosis and possible treatment,

ANEUPLOIDY (SE)

- Aneuploidy involves the loss or gain of one or more chromosomes.
- Loss of a single chromosome is called monosomy.
- Gain of one or two chromosomes is called trisomy, tetrasomy respectively.
- Depending on the type of chromosome involved it is classified as
    - **Autosomal monosomy**- loss of one autosome, but the conception is not viable.
    - Sex chromosomal monosomy- loss of one sex chromosome. Eg- Turner syndrome (45,X)
    - **Autosomal trisomy**- gain of one autosome. Eg- Down syndrome (47,XX+21; 47,XY+21)
    - **Sex chromosomal trisomy**- gain of one sex chromosome. Eg- Klinefelter syndrome (47,XXY)

X CHROMOSOME (SE)

- The X chromosome is one of the two sex-determining chromosomes and is found in both males and females.
- It is submetacentric chromosome classified under 'C' group chromosomes
- Females have two X chromosomes, whereas males have one X and one Y chromosome.
- Both males and females retain one of their mother's X chromosomes, and females retain their second X chromosome from their father.

- Early in embryonic development in females, one of the two X chromosomes is randomly and permanently inactivated in nearly all somatic cells. This phenomenon is called X-inactivation or Lyonization. The inactive X- chromosome is tightly coiled and hence stains dark purple and is seen as Barr body within the nucleus of a female. The X chromosome is notably larger and has a more active euchromatin region.
- Numerical alteration in Sex chromosomes result in abnormalities eg Turner's syndrome (XO), Klinefelter's syndrome (XXY) and Triple X syndrome (XXX).
- , Sex linked Inherited disorders both dominant and recessive also may occur.

Y CHROMOSOME (SE)

- The Y chromosome is one of the two sex chromosomes in humans (the other is the X chromosome).
- The sex chromosomes form one of the 23 pairs of human chromosomes in each cell.
- The Y chromosome is present in males, who have one X and one Y chromosome.
- Sex is determined by the SRY gene on the Y chromosome, which is responsible for the development of a fetus into a male.
- Other genes on the Y chromosome are important for male fertility. Many genes are unique to the Y chromosome.
- Genes present in areas known as pseudoautosomal regions take part in pairing during meiosis.

SEX LINKED INHERITANCE (SE)

a. X- linked dominant (X-LD) inheritance:
    - Uncommon, but disorders, manifest in the heterozygous female as well as in the male, with the mutant allele on his single X chromosome.
    - An excess of affected females may be seen in families with X-LD disorders.
    - A mosaic pattern demonstrated in affected heterozygous females for some X-LD disorders.
    - Both the daughters & the sons of an affected female with X-LD disorder, have 1 in 2 (50%) chance of being affected.
    - Affected male transmit the trait to the daughters but none to his sons.
    - Examples: Vitamin D-resistant rickets, Incontinentia pigmenti.
b. X-linked recessive(X-LR) inheritance:
    - It usually manifests only in males.
    - A male with a mutant allele on his single X is called hemizygous.
    - A male can't transmit X-linked trait to his son.
    - X-linked recessive diseases are transmitted by healthy heterozygous female carriers to male.

- Trait is transmitted to male grandchild through the obligate carrier daughters. This type of pedigree is referred to as a 'diagonal or a knight's move' pattern of transmission.
- In hetrozygous females, variable expression seen.
- A male transmits his X to his daughters & Y to his sons.
- For an affected male with a normal female: all daughters will be obligate carrier, but none of the sons will be affected.
- For a carrier female with a normal male, each son has a 1 in 2 (50%) chance of being affected & each daughter has 1 in 2 (50%) chance of being obligate carrier.
- Examples: Haemophilia, DMD (Duchenne Muscular Dystrophy).

c. Y-linked inheritance / Holandric inheritance:
   - Y- linked or holandric inheritance implies that only males are affected.
   - Affected male transmits Y –linked trait to all his sons, but none to the daughters.

CRI DU CHAT SYNDROME (SE)

- It means "cry of the cat". It is also called 5p syndrome
- Cri-du-chat is one of the most common syndromes caused by a chromosomal deletion. It affects between 1 in 20,000 and 1 in 50,000 babies.
- Cri-du-chat is caused by a deletion on the short arm of chromosome 5 (5p-).
- It usually becomes less noticeable as the baby gets older, making it difficult for doctors to diagnose Cri-du-chat after age two.
- Characteristic features: microcephaly, severe speech and motor delays, behavioural problem, intellectual disability
- Although there is no real treatment for cri-du-chat syndrome, children with the disorder can go through therapy to improve their language skills, motor skills, and to help them develop as normally as possible.

AUTOSOMAL DOMINANT INHERITANCE (SE)

- Trait is expressed even when individual has one abnormal allele (heterozygous state).
- Males and females are equally affected.
- If one parent is affected, each of their children has a 50% chance of being affected.
- If one parent is homozygous for the dominant allele, all of the children will express the trait.
- It can be traced through many generations and is called vertical transmission
- All form of transmission seen- male to male, male to female, female to female, female to male
- Examples: Achondroplasia, osteogenesis imperfecta, polydactyly, Marfan's syndrome, and some neuromuscular disorders.

PRENATAL DIAGNOSIS- PURPOSE AND METHODS (SE)

- Prenatal diagnosis is the ability to detect abnormalities in an unborn child.
- Without knowledge gained by prenatal diagnosis, there could be an untoward outcome for the fetus or the mother or both.
- Congenital anomalies account for 20 to 25% of perinatal deaths.
- Specifically, prenatal diagnosis is helpful for:
    - Managing the remaining weeks of the pregnancy,
    - determining the outcome of the pregnancy,
    - planning for possible complications with the birth process,
    - planning for problems that may occur in the newborn infant,
    - deciding whether to continue the pregnancy
    - finding conditions that may affect future pregnancies.
- There are a variety of non-invasive and invasive techniques available for prenatal diagnosis. Each of them can be applied only during specific time periods during the pregnancy for greatest utility.

Some of the techniques employed for prenatal diagnosis include:

- Ultrasonography
- Amniocentesis
- Chorionic villus sampling
- Fetal blood cells in maternal blood
- Maternal serum alpha-fetoprotein

TRISOMY 18 (SE)

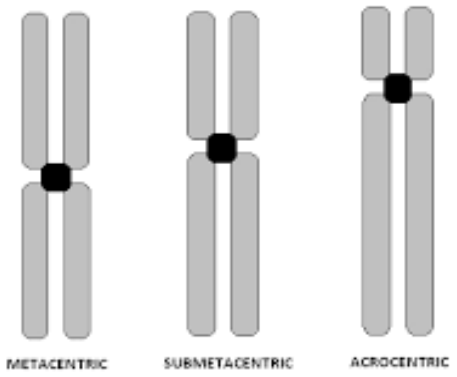
Edward syndrome (trisomy 18, 47,XX+18 or 47,XY+18**):** numerical chromosomal abnormality, autosomal trisomy.

Features are

- Infants usually die in the first few weeks after birth
- Delayed developmental milestones
- Mental retardation
- Prominent occiput
- Short palpebral fissures
- Narrow palatal arch
- Micrognathia
- Clenched hands with over-riding of fingers.
- Short sternum
- Umbilical or inguinal hernia
- Congenital heart defects

Chromosome

- Each chromosome is made up of condensed DNA which is tightly coiled many times around proteins called histones and visible under metaphase stage.
- Each chromosome has a constriction point called the centromere, which divides the chromosome into two "arms." The short arm of the chromosome is labeled the "p arm" and the long arm "q arm."
- Depending on the position of centromere the chromosomes are classified morphologically into
    - Metacentric- centromere is in the center of chromosome, where length of two arms is equal. Chromosomes 1, 3, 16, 19
    - Submetacentric- centromere is away from the center of chromosome, where one arm is shorter than the other arm. Chromosomes 2, 4, 5, 6 to 12, 17, 18, X
    - Acrocentric – centromere is towards one end of the chromosome, where one of the arms is too short and the other arm is too long. Chromosomes 13, 14, 15, 20, 21, Y
- Depending upon the length, position of centromere, bands, they are classified into 7 groups. Group A- 1, 2, 3; group B- 4, 5; group C- 6-12, X; group D- 13, 14, 15; group E- 16, 17, 18; group F- 19, 20; group G- 21, 22, Y



SEX CHROMOSOMES (SE)

- Sex chromosomes are sex determining chromosomes in males and females. In males the sex chromosomes are XY, in females it is XX.
- Both males and females retain one of their mother's X chromosomes, and females retain their second X chromosome from their father.
- The X chromosome is notably larger and has a more active euchromatin region.
- Because only males have the Y chromosome, the genes on this chromosome tend to be involved in male sex determination and development.
- Genes in areas known as pseudoautosomal regions are present on both sex chromosomes. As a result, men and women each have two functional copies of these genes. Many genes in the pseudoautosomal regions are essential for normal development.

KARYOTYPING (SE)

- The orderly arrangement of the chromosomes according to length, position of centromere, banding pattern is called karyotyping.
- A karyotype refers to a full set of chromosomes from an individual which can be compared to a normal karyotype for the species via genetic testing.
- A chromosome anomaly may be detected or confirmed in this manner.

Procedure:

- Peripheral blood is collected in a heparinized syringe.
- Blood is cultured in a suitable medium with addition of phytohaemagglutinin.
- The culture vials are incubated for three days
- Colchicine is added after 3days which arrests the WBC'S in metaphase.
- The contents are centrifuged and cells are separated and treated with hypotonic solution.This makes the cells swell up and disperse the chromosomes. These are dropped onto a chilled slide stained with Trypsin Giemsa stain.
- Metaphase spreads are analysed under microscope where each chromosome is identified for the abnormality, then photographed, cut and pasted in order.
- Chromosomes are classified into 7 groups and pasted accordingly- Group A- 1, 2, 3; group B- 4, 5; group C- 6-12, X; group D- 13, 14, 15; group E- 16, 17, 18; group F- 19, 20; group G- 21, 22, Y
- Recently there is automatic karyotyping system available where the software does the necessary karyotyping, but there should be manual checking before reporting.

Abnormalities of chromosome

- Chromosome anomalies usually occur when there is an error in cell division following meiosis or mitosis. There are many types of chromosome anomalies. They can be organized into three basic groups,
    - ✓ Numerical anomalies
    - ✓ structural anomalies
    - ✓ mosaicism.

Numerical anomalies

When it involves the loss or gain of one or more chromosomes, it is called aneuploidy. When it involves one or more sets of chromosomes it is called polyploidy. Example- Turner syndrome (XO), Klinefelter syndrome(XXY), Down syndrome (trisomy 21)

Structural anomalies

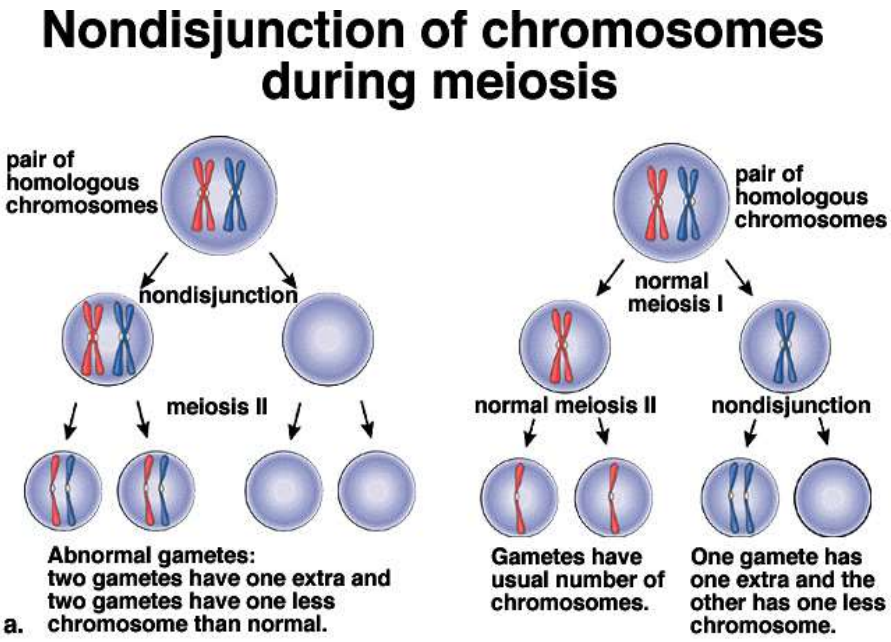
a part of the chromosome is lost or gained. When chromosome complement is complete with no loss or gain of genetic material, it is called balanced structural abnormality which is usually harmless. When chromosome complement contains less or more amount of genetic material, it is called unbalanced structural abnormality. Different types of structural abnormalities are- translocation, deletion, duplication, insertion, inversion, ring, isochromosome

Mosaicism:

is defined as presence of two or more cell lines in an individual or in a tissue that differ in genetic constitution but derived from a single zygote. It usually results from non-disjunction in an early embryonic mitotic division with the persistence of more than one cell line. For example, the two chromatids of chromosome 21 fails to separate at the second meiotic division in a human zygote, it would result in four cell zygote having two cells with 46 chromosomes, one cell with 47 chromosomes and one cell with 45 chromosomes.

Non-disjunction

- Failure of separation of homologous chromosomes in meiosis 1 or sister chromatids in meiosis 2 / mitosis during anaphase is called non-disjunction.
- If non disjunction occurs during meiosis, one daughter cell will have one extra chromosome (24) and the other will have one chromosome less (22). The daughter cell with one extra chromosome fertilizes with normal gamete it leads to trisomy and the daughter cell with one chromosome less fertilizes with normal gamete it leads to monosomy in the offspring.



- If non disjunction occurs during mitosis it leads to mosaicism.

DOWN SYNDROME / TRISOMY 21 (SE)

Down syndrome (trisomy 21, 47,XX+21 or 47,XY+21): numerical chromosomal abnormality, autosomal trisomy. Features are

- Delayed developmental milestones
- Mental retardation
- Hypotonia
- Brachycephaly
- Open mouth & protruding tongue
- Upward slant of palpebral fissures
- Inner epicanthic folds
- Small nose with flat nasal bridge
- Short neck
- Simian crease in palm
- Wide gap between 1st & 2nd toes
- Congenital heart defects – septal defects
- Infertility in male
- Fertility rare in female

KLINEFELTER SYNDROME (SE)

Klinefelter syndrome (47,XXY): numerical chromosomal abnormality, sex chromosomal trisomy. Features are

- Tall & slim
- I.Q. variable (85 to 90)
- Hypogonadism
- Hypogenitalism
- Gynaecomastia
- Low testosterone values
- Infertility
- Poor 2° sexual features
- Behavioral problems
- Karyotype: 47,XXY - 80%, 48,XXXY or 46,XY/47,XXY - 20%.

TURNER SYNDROME (SE)

- Turner syndrome numerical chromosomal abnormality, sex chromosomal monosomy. (45,X):

Features are

- Short stature
- Moderate I.Q. (90)
- Congenital lymphoedema
- Broad chest with widely spaced hypoplastic nipples

- Short, webbed neck with low posterior hairline
- Cubitus valgus
- Renal abnormalities
- Streak ovaries in USG
- Poor secondary sexual features

Mutation

- Mutation is a permanent change of the nucleotide sequence of the human genome elements.
- Mutations result from damage to DNA which is not repaired or to RNA genomes (typically caused by radiation or chemical mutagens), errors in the process of replication, or from the insertion or deletion of segments of DNA by mobile genetic elements.
- Mutations may or may not produce discernible changes in the observable characteristics (phenotype) of an organism.
- Mutations play a part in both normal and abnormal biological processes including: evolution, cancer, and the development of the immune system, including junctional diversity.
- Mutation can result in several different types of change in sequences.
- Mutations in genes can either have no effect, alter the product of a gene, or prevent the gene from functioning properly or completely.

X CHROMOSOME (SA)

- The X chromosome is one of the two sex-determining chromosomes found in both males and females.
- Females have two X chromosomes, whereas males have one X and one Y chromosome.
- Both males and females retain one of their mother's X chromosomes, and females retain their second X chromosome from their father.
- Since the father retains his X chromosome from his mother, a human female has one X chromosome from her paternal grandmother (father's side), and one X chromosome from her mother.

Y CHROMOSOME (SA)

- The Y chromosome is one of the two sex chromosomes in humans (the other is the X chromosome).
- Because only males have the Y chromosome, the genes on this chromosome tend to be involved in male sex determination and development.
- Sex is determined by the SRY gene on the Y chromosome, which is responsible for the development of a fetus into a male

- Genes in areas known as pseudoautosomal regions are present on both sex chromosomes. As a result, men and women each have two functional copies of these genes. Many genes in the pseudoautosomal regions are essential for normal development.

GENETIC CODE (SA)

- The genetic code is the set of rules by which information encoded within genetic material (DNA or mRNA sequences) is translated into proteins by living cells.
- Biological decoding is accomplished by the ribosome, which links amino acids in an order specified by mRNA, using transfer RNA (tRNA) molecules to carry amino acids and to read the mRNA three nucleotides at a time.
- The genetic code is highly similar among all organisms and can be expressed in a simple table with 64 entries.
- The code defines how sequences of these nucleotide triplets, called *codons*, specify which amino acid will be added next during protein synthesis.

GENETIC COUNSELING (SA)

- It is a process of communication and education that addresses concerns relating to the development and / or transmission of a hereditary disorder.
- An individual who seeks genetic counseling is called consultand and person who gives counseling is called counselor.
- The steps in genetic counseling are- diagnosis, risk assessment, discussion of options, communication, long term contact and support.
- During the process,the consultand are advised about
  (1) the nature and the results of the disorder
  (2) the chances of developing / transmitting the disorder
  (3) the options for the management of the disorder so as to prevent , avoid or improve the outcome of the disorder.
- The counseling should be non-directive approach.

WHAT IS THE DIFFERENCE BETWEEN METACENTRIC, SUBMETACENTRIC AND ACROCENTRIC CHROMOSOMES? (SA)

chromosomes are classified according to the position of the centromere.

- **Metacentric**
  centromere is in the center of chromosome, where length of two arms is equal. Chromosomes 1, 3, 16, 19
- **Submetacentric**
  centromere is away from the center of chromosome, where one arm is shorter than the other arm. Chromosomes 2, 4, 5, 6 to 12, 17, 18,and X chromosome

- **Acrocentric**

  centromere is towards one end of the chromosome, where one of the arms is too short and the other arm is too long. Chromosomes 13, 14, 15, 20, 21 and Y chromosome

LIST SIX ACROCENTRIC CHROMOSOMES (SA)

Centromere is towards one end of the chromosome, where one of the arms is too short and the other arm is too long. Chromosomes 13, 14, 15, 20, 21 and Y chromosome.

METACENTRIC CHROMOSOMES- GROUP AND NUMBER (SA)

Metacentric- centromere is in the center of chromosome, where length of two arms is equal. Chromosomes 1, 3, 16, 19

RING CHROMOSOMES (SA)

- Telomeres of two ends are lost and the sticky ends join with each other to form ring chromosome.
- A ring chromosome is denoted by the symbol '**r**' in human genetics.
- Ring chromosomes may form in cells following genetic damage by mutagens like radiation, but they may also arise spontaneously during development.
- Although ring chromosomes are very rare, they have been found in nearly all human chromosomes.
- Disorders arising from the formation of a ring chromosome include ring chromosome 20 syndrome (epilepsy); ring chromosome 14 and ring chromosome 13 syndrome (mental retardation and dysmorphic facial features)

SATELLITE BODIES (SA)

- Besides the centromere, one or more secondary constrictions can also be observed in some chromosomes at metaphase called as satellite body.
- The secondary constrictions are always constant in their positions and hence can be used as markers that identify particular chromosomes.
- If the secondary constriction contains the nucleolus organizer region, the chromosome is called a nucleolar satellite chromosome
- In humans, chromosomes number **13, 14, 15, 21 and 22** are examples of satellite chromosomes

ANAPHASE LAG (SA)

- Anaphase lag describes a delayed movement of chromosome or chromatid during anaphase.
- One homologous chromosome in meiosis or one chromatid in mitosis fails to connect to the spindle apparatus and is lost without entering any of the daughter cell.
- The lagging chromosome is not incorporated into the nucleus of one of the daughter cells, resulting in one normal daughter cell and one with monosomy.

- Anaphase lag is one cause of aneuploidy. Anaphase lag can also cause a rescue of the daughter cell if the cell was originally trisomy

MENTION ANY THREE STRUCTURAL ABNORMALITIES OF CHROMOSOMES (SA)

- Translocation- rearrangement of parts between nonhomologous chromosomes.
  Eg. Down syndrome (21/22)
- Deletion- a segment of the chromosome is deleted Eg. Cri du chat syndrome
- Duplication- a segment of the chromosome is duplicated Eg. Di George syndrome 22q11.2

SATELLITE CHROMOSOMES (SA)

- Besides the centromere, one or more secondary constrictions can also be observed in some chromosomes at metaphase called as satellite body.
- The secondary constrictions are always constant in their positions and hence can be used as markers that identify particular chromosomes.
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- In humans, chromosomes number **13, 14, 15, 21 and 22** are examples of SAT chromosomes

NAME THE CHROMOSOMES WITH SATELLITE BODIES (SA)

- Besides the centromere, one or more secondary constrictions can also be observed in some chromosomes at metaphase called as satellite body .In humans, chromosomes number **13, 14, 15, 21 and 22** are examples of satellite chromosomes

ROBERTSONIAN TRANSLOCATION (SA)

- Rearrangement of chromosomal segments between two acrocentric chromosomes is called Robertsonian translocation.
- Acrocentric chromosomes are- **13, 14, 15, 21 and 22**
- The translocation will be usually between chromosomes 14 and 21
- Eg.Down syndrome (14/21)

ANEUPLOIDY (SA)

- Loss or gain of one chromosome is called as aneuploidy.
- Loss of one chromosome is called monosomy, gain of one or more chromosomes is called trisomy or polysomy respectively.
- Examples- monosomy-Turner syndrome(45,X); trisomy- Down syndrome, Klinefelter syndrome

MENTION EXAMPLES OF X LINKED RECESSIVE INHERITANCE (SA)

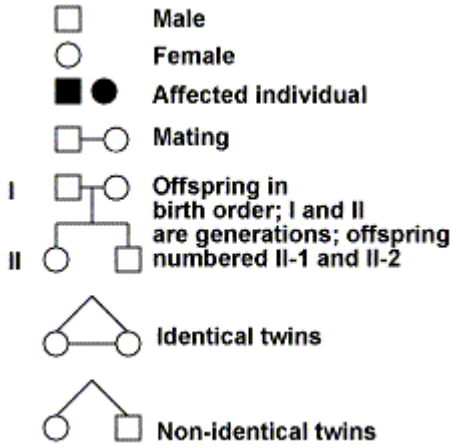
X-linked recessive diseases are transmitted by healthy heterozygous female carriers to male

- Haemophilia
- DMD (Duchenne Muscular Dystrophy)
- Ocular albinism
- Red-green color blindness

WHAT IS PEDIGREE ANALYSIS? (SA)

- Pedigrees are charts of family histories that show the phenotypes and family relationships of the individuals using symbols to represent different family members.

The investigator traces the history of some variant phenotype back through the history of the family and draws up a family tree, or pedigree, using the standard symbols.



POLYPLOIDY (SA)

- An individual containing more than two paired (homologous) sets of chromosomes is called polyploidy.
- Gain of one complete set of chromosomes is called triploidy. Total number of chromosomes are 69
- Gain of two complete sets of chromosomes are called as tetraploidy with total number of chromosomes 92.

TRANSLOCATION (SA)

- Translocation is the rearrangement of parts between nonhomologous chromosomes.
- No loss or gain of genetic material is balanced translocation and with less or more of genetic material is unbalanced translocation leading to abnormality.
- Two types of translocations are reciprocal and Robertsonian translocation
- Reciprocal translocation: it is formed when a break occurs in each of two chromosomes with the segments being exchanged to form to form two new derivative chromosomes.

- Robertsonian translocation: it is a particular type of reciprocal translocation in which breaking points are located at, or close to , centromeres of two acrocentric chromosomes.

NAME ANY TWO CONDITIONS AFFECTING AUTOSOMES (SA)

- Down syndrome (47,XX+21)
- Cri du chat syndrome (deletion 5 syndrome)
- Angelman / Prader willi syndrome (microdeletion in chromosome 15)

DOWN SYNDROME (SA)

Karyotype- 47,XX+21; 47,XY+21, numerical chromosomal abnormality

- Delayed developmental milestones
- Mental retardation
- Hypotonia
- Brachycephaly
- Open mouth & protruding tongue
- Upward slant of palpebral fissures
- Inner epicanthic folds
- Small nose with flat nasal bridge
- Small ears
- Short neck
- Simian crease in palm

NAME ANY THREE AUTOSOMAL DOMINANT DISORDERS (SA)

Autosomal dominant inheritance refers to conditions caused by changes ("mutations") in genes located on one of the 22 pairs of autosomes

Porphyria Variegata
Polydactyly
Tuberous sclerosis
Achondroplasia
Neurofibromatosis type 1
Osteogenesis imperfecta

DEFINE GENOTYPE AND PHENOTYPE (SA)

- Genotype: is the genetic constitution of the individual which is fixed at the time of fertilization.

- Phenotype: is the appearance of an individual resulting from the interaction of genotype & environment. It is the physical or biochemical expression of the genotype. Phenotype is potentially variable.

AUTOSOMAL DOMINANCE (SA)

- Trait is expressed even when individual has one abnormal allele (heterozygous state).
- Males and females are equally affected.
- If one parent is affected, the child has a 50% chance of being affected and 50% chance of being normal.
- It can be traced through many generations and is called vertical transmission
- All form of transmission seen- male to male, male to female, female to female, female to male
- Examples: Achondroplasia, osteogenesis imperfecta, polydactyly

NAME ANY FOUR AUTOSOMAL RECESSIVE DISORDERS (SA)

An autosomal recessive disorder means two copies of an abnormal gene must be present in order for the disease or trait to develop.

- Cystic fibrosis
- Alkaptonuria
- Albinism
- Sensorineuronal
- Hearing impairment / deafness
- Beta thalassaemia

NAME THE TYPES OF CHROMOSOMES (SA)

- **Metacentric**

  centromere is in the center of chromosome, where length of two arms is equal. Chromosomes 1, 3, 16, 19
- **Submetacentric**
  - centromere is away from the center of chromosome, where one arm is shorter than the other arm. Chromosomes 2, 4, 5, 6 to 12, 17, 18, X
- **Acrocentric**
  - centromere is towards one end of the chromosome, where one of the arms is too short and the other arm is too long. Chromosomes 13, 14, 15, 20, 21, Y

PRENATAL DIAGNOSIS (SA)

- Prenatal diagnosis is the ability to detect abnormalities in an unborn child.
- Specifically, prenatal diagnosis is helpful for: Managing the remaining weeks of the pregnancy, determining the outcome of the pregnancy, planning for possible complications with the birth

process, planning for problems that may occur in the newborn infant, deciding whether to continue the pregnancy and finding conditions that may affect future pregnancies.

- There are a variety of non-invasive and invasive techniques available for prenatal diagnosis. Each of them can be applied only during specific time periods during the pregnancy for greatest utility.
- *Some of the techniques employed for prenatal diagnosis include:*
    - Ultrasonography
    - Amniocentesis
    - Chorionic villus sampling

NAME ANY TWO PRENATAL DIAGNOSTIC PROCEDURES (SA)

- Ultrasonography
- Amniocentesis
- Chorionic villus sampling

CHROMOSOME (SA)

- Each chromosome is made up of condensed DNA which is tightly coiled many times around proteins called histones and visible under metaphase stage.
- It has a constriction point called the centromere, which divides the chromosome into two "arms" - short arm (p arm) and long arm (q arm).
- Depending on the position of centromere the chromosomes are classified morphologically into metacentric, submetacentric and acrocentric chromosomes

SEX CHROMOSOMES (SA)

- Sex chromosomes are sex determining chromosomes in males and females. In males the sex chromosomes are XY, in females it is XX.
- The X chromosome in humans is submetacentric belonging to 'C' group.
- The X chromosome is notably larger and has a more active euchromatin region.
- The Y chromosome is acrocentric and belongs to 'G' group.
- Because only males have the Y chromosome, the genes on this chromosome tend to be involved in male sex determination and development.

RECESSIVE GENES (SA)

- A gene that is phenotypically expressed in the homozygous state but has its expression masked in the presence of a dominant gene is called recessive gene.
- The person with one normal and one recessive gene will not express any abnormal features and is called as carrier.

- The recessive genes are expressed in the individuals of same generation leading to horizontal transmission.
- Examples- Cystic fibrosis, Alkaptonuria, Albinism

GENOME (SA)

- A genome is an organism's complete set of DNA, including all of its genes.
- Each genome contains all of the information needed to build and maintain that organism.
- In humans, a copy of the entire genome—more than 3 billion DNA base pairs—is contained in all cells that have a nucleus.
- The genome includes both the genes and the non-coding sequences of the DNA/RNA
- The Human Genome Project was an international research effort to determine the sequence of the human genome and identify the genes that it contains.

AUTOSOMES (SA)

- An autosome is a chromosome not involved in sex determination and is numbered.
- Humans have 22 pairs of autosomes and one pair of sex chromosomes (the X and Y)
- Autosomal dominant genes are expressed in heterozygous state.
- Autosomal recessive genes are expressed in homozygous state.

Define chromosome. Give the chromosome complement of normal male and female (SA)

- Chromosome is condensed DNA which is tightly coiled many times around proteins called histones and visible under metaphase stage.
- Normal male complement: 46,XY
- Normal female complement: 46,XX

KARYOTYPE (SA)

- A karyotype refers to a full set of chromosomes from an individual arranged according to length, position of centromere, banding pattern.
- Karyotype is written as total number of chromosomes followed by sex chromosomes
- Normal male karyotype: 46,XY, normal female karyotype: 46,XX
- Chromosomes are classified into 7 groups and pasted accordingly- Group A- 1, 2, 3; group B- 4, 5; group C- 6-12, X; group D- 13, 14, 15; group E- 16, 17, 18; group F- 19, 20; group G- 21, 22, Y

KARYOTYPING (SA)

- Karyotyping is a laboratory technique used to analyse chromosomes in order to look for any major chromosomal anomaly which may cause a genetic condition.

- The technique includes setting up of culture, harvesting, preparation of slides, staining, analyzing the metaphase spreads and arranging chromosomes according to length, position of centromere, banding pattern.

WRITE ANY THREE DIFFERENCES BETWEEN MITOSIS AND MEIOSIS (SA)

	Mitosis	Meiosis
Site of occurrence	Somatic cells	Gametic cells
Cell cycle	One cycle	Two cycles-meiosis 1and meiosis 2
Prophase	Short duration	Prolonged in meiosis 1
Pairing and crossing over	Absent	Present
Duration per cycle	24 hours	60-65 days in male, 12 to 50 years in females
Chromosome complement	Diploid	Reduced to half - haploid
Produces	Two daughter cells	Four daughter cells

MEIOSIS (SA)

- It is the process of nuclear division that occurs during the final stage of gamete formation.
- It has two cell divisions- meiosis 1 which is reductional division and meiosis 2 which is equational division resulting in 4 daughter cells.
- Prophase 1 is longer and has 5 stages-leptotene, zygotene, pachytene, diplotene and diakinesis
- The chromosomal complement is reduced to haploid set of chromosomes (n-23)
- Duration to complete one meiosis varies from few days to years

SIGNIFICANCE OF MEIOSIS (SA)

- Reductional division- the child gets half of its chromosomes from each parent
- Provides genetic diversity.
- Separation of chromosomes follows law of independent assortment where each gamete receives a selection of parental chromosomes. The chance of getting same chromosomes in two gametes is approximately 1 in 8 million.
- Because of crossing over each chromatid receives DNA derived from both parental homologous chromosomes referred to as gene shuffling

SIMIAN PALMAR CREASE (SA)

- In humans, a single transverse palmar crease is a single crease that extends across the palm of the hand, formed by the fusion of the two palmar creases.
- It is associated with few abnormal genetic conditions like Down syndrome, Patau syndrome, Edward syndrome, Cri du chat syndrome

NAME ANY THREE SYNDROMES HAVING TRISOMY (SA)

A condition in which an extra copy of a chromosome is present in the cell nuclei, causing developmental abnormalities.

- Trisomy 13 (Patau syndrome)
- trisomy 21 (Down syndrome)
- trisomy 18 (Edward syndrome)

NON-DISJUNCTION (SA)

- It is the failure of separation of one of the pairs of homologous chromosomes during anaphase of meiosis or mitosis.
- if it occurs during meiosis it leads to monosomy or trisomy after fertilization.
- If it occurs during mitosis it leads to mosaicism.

DOWN SYNDROME-KARYOTYPE AND CLINICAL FEATURES (SA)

Karyotype- 47,XX+21; 47,XY+21, numerical chromosomal abnormality

- Delayed developmental milestones
- Mental retardation
- Hypotonia
- Brachycephaly
- Open mouth & protruding tongue
- Upward slant of palpebral fissures
- Inner epicanthic folds
- Small nose with flat nasal bridge
- Small ears
- Short neck
- Simian crease in palm

GENOTYPE OF DOWN SYNDROME (SA)

- 47,XX+21
- 47,XY+21
- Translocation down 46,XX,t(14;21)

TRISOMY (SA)

- A trisomy is a type of aneuploidy in which there are three copies of a particular chromosome, instead of the normal two.
- Depending upon the type of chromosome involved it is classified as autosomal trisomy and sex chromosomal trisomy.

- Examples- autosomal trisomy- Down syndrome (trisomy 21), sex chromosomal trisomy- Klinefelter syndrome (47,XXY)

KLINEFELTER SYNDROME – KARYOTYPE AND CLINICAL FEATURES (SA)

Numerical chromosomal abnormality, sex chromosomal trisomy. 47,XXY

Clinical Features are:

- Tall & slim
- I.Q. variable (85 to 90)
- Hypogonadism
- Hypogenitalism
- Gynaecomastia
- Low testosterone values
- Infertility
- Poor secondary sexual features
- Behavioral problems

MONOSOMY (SA)

- Monosomy is a form of aneuploidy with the presence of only one chromosome from a pair.
- Partial monosomy occurs when only a portion of the chromosome has one copy, while the rest has two copies
- Examples- Turner syndrome (45,X), Cri du chat syndrome (deletion 5p syndrome)

TURNER SYNDROME- KARYOTYPE AND CLINICAL FEATURES (SA)

Numerical chromosomal abnormality, sex chromosomal monosomy (XO)

Clinical Features are:

- Short stature
- Moderate I.Q. (90)
- Congenital lymphoedema
- Broad chest with widely spaced hypoplastic nipples
- Short, webbed neck with low posterior hairline
- Cubitus valgus
- Renal abnormalities
- Streak ovaries in USG
- Poor secondary sexual features

WHAT IS THE CAUSE OF TURNER SYNDROME (SA)

- It is the result of non-disjunction of sex chromosomes during anaphase of meiosis, especially during paternal gametogenesis .
- The daughter cell which does not receive any of the sex chromosome after fertilization with normal gamete having X chromosome results in Turner syndrome.

TWO SYNDROMES AFFECTING SEX CHROMOSOMES (SA)

- Turner syndrome (45,X)
- Klinefelter syndrome (47,XXY)
- Triple X syndrome (47,XXX)

MUTATION (SA)

- It is defined as heritable alteration or change in the genetic material.
- It can arise through exposure to mutagenic agents which include natural or artificial ionizing radiation and chemical or physical mutagens. But majority occur spontaneously through errors in DNA replication and repair.
- Two types- somatic mutation which cannot be transmitted to offspring, mutation in gametes can be transmitted to future generations

RECESSIVE TRAIT (SA)

- Recessive trait is a condition which is expressed in the individual in the presence of two copies of recessive genes in homozygous form.
- In heterozygous form i.e, one recessive gene and one abnormal gene there is no expression of the trait and the individual is called carrier
- Example- Cystic fibrosis, Alkaptonuria, Albinism

WHAT IS PHILADELPHIA CHROMOSOME? (SA)

- Philadelphia chromosome is the chromosome with translocation between 9 and 22.
- This chromosome is defective and unusually short because of reciprocal translocation of genetic material between chromosome 9 and chromosome 22, and contains a fusion gene called BCR-ABL1
- It is associated with the condition myeloid leukemia.
- It was the first consistent chromosome abnormality found in any kind of malignancy

GIVE TWO INDICATIONS FOR AMNIOCENTESIS (SA)

The prenatal test is generally offered to women who

- have a significant risk for genetic diseases
- have an abnormal ultrasound

- have a family history of certain birth defects
- have previously had a child with birth defect
- will be more than 35 years of age

CHROMOSOME BANDING (SA)

- The chromosomes should be stained before analyzing them.
- Staining gives the chromosomes light and dark bands which are specific to particular chromosome which makes analysis easy to identify each and every chromosome and also any abnormality.
- There are different banding techniques, but routine banding is G- banding technique
  Other banding techniques are Q- banding, R- banding and C- banding.