COMPLEX MULTIGENETIC DISORDERS.

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Gene.

- Basic physical and functional unit of heredity.
- Made up of DNA.
- **Genes** influence many of our characteristics including the likelihood of developing disease.

- **Alleles**: Form of the same gene with small differences in their sequence of DNA bases.

Diseases.

- Hereditary→ Pass from parents to their offspring.

- Familial→ Run in families and represent examples of multifactorial(polygenic) inheritance.

- Congenital→ Present by birth.

Congenital Diseases.

- May be due to structural changes in DNA (Mutations) ;
- Or by direct injury to fetus in utero.
- e.g. Anencephaly, Down syndrome, Klinefilter syndrome, TORCH complex, Cleft lip with/without cleft palate.

Normal Human Karyotype.

- Somatic cells→ 22 pairs autosomes & 2 sex chromosomes (46,XX or 46, XY).
- Diploid (2 copies of each chromosome).

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- Sperm and eggs carry 23 chromosomes and are haploid(carry 1 copy of each chromosome).

- Sperm determines genotypic sex (either an X or a Y chromosome).

Complex Multigenetic Disorders.

- They are likely associated with the effects of multiple genes (polygenic) in combination with lifestyle and environmental factors.
- E.g. Heart **diseases**, Type 2 DM and obesity.

- Governed by additive effect of 2 or more genes of small effect conditioned by environmental, nongenetic influences.

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- Involved in many of physiologic characteristics of humans like height,weight,BP,hair color.

- e.g. Monozygous twins→different nutrition & environmental influences→different heights.

Main features.

- Severity of disease ∝ No. & Degree of influence of inherited pathologic or mutant genes.
- Environmental factors influence expression of clinical symptoms.

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- Greater risk in siblings of patients and close relatives having severe expressions of disorder.

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- The more severe the symptoms, the greater the risk of transmitting this trait to offspring.

- Some diseases show sex predilection as congenital pyloric stenosis occurs 5 times more frequently in males than females.

Rate of Recurrence of disease.

- Tend to run in families.
- 2-7 % for all 1st degree relatives.
- i.e. parents, siblings and offsprings of affected individual.

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- When 1 child is affected, there is as high as a 7 % chance that the next child will be affected.

- After 2 affected siblings, risk rises to about 9 %.

Diseases.

- DM type 2,
- HTN,
- Gout,
- Schizophrenia,

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- Cleft lip and cleft palate,
- Bipolar disorder,
- Certain forms of congenital cardiac diseases,
- Some skeletal abnormalities.

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- Neural tube defects(anencephaly, meningomyelocele, spina bifida),
- Atherosclerosis,
- Pyloric stenosis.