BHARATHIDASAN UNIVERSITY

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Programme: M.Sc., Biomedical Science
(5 Year Integrated Program)

Course Title : Principles of Genetics
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Unit-III
Introduction to Clinical Genetics

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Introduction to Clinical Genetics

(Study and application of genetics to diagnose, manage, and prevent genetic disorders)

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Congenital Abnormalities and Dysmorphic Syndromes

- **Congenital Abnormalities**: Structural or functional defects present at birth.
- **Dysmorphic Syndromes**: Disorders characterized by abnormal physical development.

➢ **Congenital Abnormalities:**

1. Neural tube defects (e.g., spina bifida).
2. Cleft lip and palate.
3. Congenital heart defects (e.g., tetralogy of Fallot).

Causes: Genetic mutations, chromosomal abnormalities, environmental factors (e.g., maternal infections, drugs).

➢ **Dysmorphic Syndromes:**

1. Down Syndrome:
   Trisomy 21, characterized by flat facial features, developmental delay.
2. Turner Syndrome:
   Monosomy X, features include short stature and infertility.

- **Diagnosis**: Clinical examination, karyotyping, genetic tests.

Genetic Counselling

A process to evaluate and understand a family's risk of inherited disorders

1. Steps in Genetic Counseling:

- Family history analysis (pedigree).
- Risk assessment for genetic conditions.
- Discussion of options: testing, management, and reproduction choices.

2. Importance:

- Helps individuals make informed decisions.
- Offers emotional support.

3. Examples:

- Counseling parents with a child diagnosed with cystic fibrosis to assess risks for future pregnancies.
- Advising a family with a history of BRCA1 mutations on breast and ovarian cancer risk.

Chromosomal Breakage Syndromes

Disorders caused by increased susceptibility of chromosomes to breakage and rearrangement

1. **Examples:**
   - **Fanconi Anemia**:
     - •Features: Bone marrow failure, increased cancer risk, congenital malformations.
     - •Cause: Mutations in genes involved in DNA repair
   - **Bloom Syndrome**:
     - •Features: Short stature, photosensitivity, increased risk of cancer.
     - •Cause: Mutations in the BLM gene.
   - **Ataxia-Telangiectasia**:
     - •Features: Neurological dysfunction, immunodeficiency, and cancer risk.
     - •Cause: ATM gene mutations.
2. **Diagnosis: Cytogenetic studies, DNA damage assays.**
3. **Management: Supportive care, hematopoietic stem cell transplantation (e.g., for Fanconi anemia).**

Single Gene Disorders

(Disorders caused by mutations in a single gene)

Inheritance Patterns: Autosomal dominant, autosomal recessive, X-linked.

- **Huntington Disease**
  Cause : Trinucleotide (CAG) repeat expansion in the HTT gene.
  Symptoms : Progressive neurodegeneration, movement disorders, psychiatric symptoms.
  Inheritance : Autosomal dominant.
  Diagnosis : Genetic testing for CAG repeats.

- **Neurofibromatosis**
  Types : NF1 and NF2.
  Cause : Mutations in the NF1 or NF2 genes.
  Symptoms : Café-au-lait spots, neurofibromas, learning disabilities (NF1); hearing loss and vestibular schwannomas (NF2).
  Inheritance : Autosomal dominant.
  Example : NF1 occurs in 1 in 3,000 individuals.

- **Cystic Fibrosis**
  Cause : Mutations in the CFTR gene.
  Symptoms : Thick mucus production, respiratory infections, pancreatic insufficiency.
  Inheritance : Autosomal recessive.
  Diagnosis : Sweat chloride test, CFTR gene mutation analysis.

Single Gene Disorders . . .

(Organized structures of DNA, carrying genetic information)

- **Cardiomyopathies**
  Types : Hypertrophic, dilated, restrictive.
  Cause : Mutations in genes encoding sarcomeric proteins (e.g., MYH7).
  Symptoms : Heart failure, arrhythmias.
  Inheritance : Often autosomal dominant.
  Example : Hypertrophic cardiomyopathy affects 1 in 500 individuals.

- **Duchenne Muscular Dystrophy (DMD)**
  Cause : Mutations in the DMD gene leading to dystrophin deficiency.
  Symptoms : Progressive muscle weakness, delayed motor milestones, cardiac complications.
  Inheritance : X-linked recessive (mostly affects males).
  Diagnosis : Elevated creatine kinase levels, genetic testing.

- **Hemophilia**
  Types : Hemophilia A (Factor VIII deficiency), Hemophilia B (Factor IX deficiency).
  Symptoms : Excessive bleeding, joint damage due to hemorrhage.
  Inheritance : X-linked recessive.
  Treatment : Clotting factor replacement therapy.

Genetic Instability

Tendency of the genome to acquire mutations due to defects in DNA repair mechanisms

1. **Causes of Genetic Instability:**

   •Errors during DNA replication.
   •Exposure to mutagens (radiation, chemicals).
   •Defective DNA repair pathways.

2. **Examples:**
   - **Lynch Syndrome**: Defects in mismatch repair genes leading to increased cancer risk.
   - **Xeroderma Pigmentosum**: Inability to repair UV-induced DNA damage.

3. **Impact:**
   - Drives cancer development and progression.