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Unit-IV
Screening of Diseases and Genetic Inheritance

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Screening of Diseases and Genetic Inheritance

(Carrier Testing, Population Screening, Probability Theory, and Risk Calculations)

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Introduction

Objective:

To understand the principles and applications of disease screening.

To explore genetic inheritance models and risk prediction tools.

Importance:

Early identification of genetic risks.

Informing clinical decisions and family planning.

Screening of Diseases

Systematic identification of individuals at risk of genetic diseases or carriers of genetic conditions.

- **Carrier Testing**

Identifies individuals who carry a mutation for a recessive genetic disorder.

Examples:

Cystic Fibrosis: Testing for mutations in the *CFTR* gene.

Sickle Cell Anemia: Screening for carriers of the sickle-cell allele in high-risk populations.

Who Benefits:

Couples planning a family.

Individuals with a family history of genetic disorders.

- **Population Screening**

  Detects diseases or carriers in the general population to reduce disease burden.

Examples:

Newborn Screening : Phenylketonuria (PKU), hypothyroidism.

Tay-Sachs Carrier Screening : Ashkenazi Jewish population.

Benefits:

Early diagnosis and treatment.

Prevention of genetic disorders in at-risk populations.

- **Genetic Registers**

  Databases to record information about individuals and families with genetic conditions.

Purpose:

Helps track inheritance patterns.

Facilitates targeted genetic counseling and research.

Example:

Register for individuals with BRCA1/2 mutations to monitor cancer risk.

Probability Theory in Genetics

Study of how likely an event is to occur, applied to predict inheritance of genetic traits

Importance:

Guides genetic counseling.

Estimates risks for specific genetic conditions.

- **Probability**:
  Likelihood of a specific outcome (e.g., 50% chance of inheriting an allele).
- **Punnett Squares**:
  Used to visualize probabilities of inheritance patterns.
  Example:
  A heterozygous parent (Aa) crossed with another heterozygous parent (Aa) has a 25% chance of producing a homozygous recessive (aa) offspring.

Applications in Carrier Testing:

If both parents are carriers of a recessive condition, there is a 25% chance their child will have the condition.

Autosomal Dominant and Recessive Inheritance

➢ Autosomal Dominant Inheritance

A single copy of the dominant allele is sufficient to express the trait.

Characteristics:

- Vertical pattern in pedigrees.
- Affected individuals have at least one affected parent.

Examples:

- Huntington's Disease.
- Marfan Syndrome.

Probability:

Affected parent (Aa) × unaffected parent (aa) → 50% chance of an affected child.

➢ Autosomal Recessive Inheritance

Both copies of the gene must be mutated for the condition to manifest.

Characteristics:

- Horizontal pattern in pedigrees.
- Affected individuals often have unaffected carrier parents.

Examples:

- Sickle Cell Anemia.
- Cystic Fibrosis.

Probability:

Carrier parent (Aa) × carrier parent (Aa) → 25% chance of an affected child.

Bayes' Theorem in Genetic Counselling

A mathematical formula used to update the probability of an event based on new information.

$$P(A|B) = \frac{P(B|A)\,P(A)}{P(B)}$$

Application in Genetics:

- Revises risk estimates based on additional data (e.g., test results).

Example:

Initial Risk: 1/4 (based on family history).

After a negative genetic test: Use Bayes' theorem to adjust the risk downward.

Clinical Use:

- Estimating carrier probabilities.
- Reassessing risk after multiple tests (e.g., negative ultrasound findings).

Empiric Risks

Risk estimates based on observed data, not theoretical models.

Importance:

Used when genetic mechanisms are unclear or complex (e.g., multifactorial disorders).

- **Examples of Empiric Risks:**
  - Recurrence risk for neural tube defects: ~2-3% if one affected child; ~10% if two affected children.
  - Recurrence risk for cleft lip and palate: ~4% if one parent is affected

- **Factors Influencing Empiric Risks:**
  - Family history (number of affected relatives).
  - Severity of the disorder.
  - Environmental influences

Case Study: Genetic Risk Assessment

Scenario:

A couple comes for genetic counseling. The woman is a carrier for cystic fibrosis (CFTR gene mutation), and her partner's genetic status is unknown.

Steps:

1.Carrier Probability for Partner:

- In the general population, carrier frequency for CF is ~1/25.

2.Risk Calculation:

- Using probability theory:
  - **Carrier parent (Aa)** × **carrier partner (Aa)** = 25% chance of an affected child.
- Bayes' theorem can revise this probability after testing the partner.

Outcome:

- If the partner tests negative, the risk is greatly reduced.
- If positive, options like IVF with genetic testing can be discussed.

- Screening programs identify carriers and at-risk individuals for genetic diseases.
- Probability theory aids in predicting inheritance patterns.
- Autosomal dominant and recessive inheritance models explain common genetic risks.
- Bayes' theorem refines risk predictions with new evidence.
- Empiric risks guide decisions when genetic mechanisms are complex or multifactorial.