Control and Prevention of Genetic Disorders

- Carrier Detection
- Genetic and Health Counselling
Over the last 1-2 decades, a significant transition has taken place in the aetiology of diseases affecting mankind where,

Environmentally related disorders have decreased and genetic disorders and non-communicable disorders have become a major cause of morbidity and mortality.
Several single gene, multifactorial and chromosomal disorders occur at a high frequency in several populations. Implementation of control and prevention programs can achieve ‘primary prevention’ i.e. prevent the birth of an affected child.
Control and prevention programmes if effectively implemented can reduce the:
- frequency of homozygous and double heterozygous states
- morbidity
- psychosocial trauma

Successful implementation of control and prevention programmes require awareness amongst:
- professionals
- community
STAGES OF PREVENTION

Primary Prevention
Secondary Prevention
Tertiary Prevention
Steps towards control and Prevention of Genetic Disorders

- **Early detection and interaction**
  - To Prevent birth of an affected child (Primary prevention)
  - To Prevent clinical manifestations in affected individuals by appropriate intervention (Secondary Prevention)
  - Provision of adequate care and rehabilitation in affected individuals (Tertiary Prevention)

- **Screening**

- **Counseling**
Control and Prevention Programmes For Genetic Diseases

Genetic Diseases (Control and Prevention)

- Increase awareness
- Genetic Screening
- Appropriate management and consultation programmes

- High risk
- Premarital
- Prenatal
- Neonatal
- General populations

Genetic Counselling

- Patients, families and community
- Clinical staff and premedical personnel
- Health policy makers and administration
PREVENTIVE SCREENING

Preclinical diagnosis of Genetic diseases

Early intervention

• Disability correction and prevention
• Reduce expression and severity of disability

Genetic Counseling

• Carrier detection
• High risk groups

Control and Prevention
Examples of primary prevention of genetic diseases

- Carrier detection
- Premarital
- Preconception
- Preimplantation

Genetic Counselling

To prevent the birth of an affected child

Vaccinating the females against Rubella

Prevention of genetic defects in the fetus

Folic acid supplementation prior to and during pregnancy

Prevention of neural tube defect in newborn
Early Detection and Intervention

• Early detection is possible for several diseases using genetic engineering techniques.
• Early and appropriate intervention plays a key role in either preventing the genetic disease or reducing the severity of its clinical manifestations.
Early diagnosis of a Genetic Disease

Pre-implantation genetic diagnosis

- Normal embryo: Implant
- Abnormal embryo: Discard

Prenatal diagnosis

Abnormal fetus

- Abnormality detected: Appropriate intervention
- Correction of defect

Newborn Screening

Carrier detection

- Genetic counselling

Abortion?
Prevention of Congenital Hypothyroidism

New born

Neonatal Screening

Hormone Replacement Therapy

Prevention of congenital hypothyroidism
Prevention Of Neural Tube Defect

Folic Acid supplementation prior to & during Pregnancy

Normal baby
Detection and Intervention of Carrier

Carrier detection

Genetic Counselling

Primary Prevention

(Prevention of birth of a child with homozygous or double heterozygous state)
Population, Premarital and preconception Screening

Objectives

To identify carriers for a particular gene defect

To identify individual with a genetic predisposition to a disease

Genetic counseling for prevention of birth of affected child

Genetic counseling to prevent or delay disease development
Autosomal Recessive Disorders Suitable for Population Screening

- $\alpha$-thal.
- $\beta$-thal.
- Hb S.
- G-6-PD deficiency.
- Cystic fibrosis.
- Tay-Sachs disease.
- Multifactorial disorders are included in several population screening programs.
Screening for carriers of recessive genetic diseases

The following criteria must be met

(I) Disease presentation is severe.
(ii) Screening is directed towards high risk population
(iii) Availability of an inexpensive sensitive and specific test.
(iv) Reproduction options are available to couples found to be at risk.
(v) Genetic counselling is available.
Examples of screening to identify individuals at increased risk of having children with genetic diseases

Screening for Hb S or β-thalassaemia

Both partners carriers

Genetic counseling

Prevent the birth of an affected child
Screening programs for β-thal. in Greece and Italy have resulted in a drop in the incidence of affected homozygotes by almost 95%.
The success of a genetic screening program can be judged on the basis of a reduction in the births of affected babies.

<table>
<thead>
<tr>
<th>Year</th>
<th>Event Description</th>
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<tbody>
<tr>
<td>1974</td>
<td>Birth incidence of β-thal. major = 1 in 250.</td>
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<tr>
<td></td>
<td>Introduction of a comprehensive screening program to determine carrier status of</td>
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<tr>
<td></td>
<td>young adults and premarital couple.</td>
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<tr>
<td>1984</td>
<td>Incidence of affected babies declined by over 95%.</td>
</tr>
<tr>
<td>1990’s</td>
<td>No new birth of a β-thal. major baby.</td>
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Screening for presymptomatic individuals at risk for adult-onset genetic disease

e.g.:
• Diabetes mellitus?
• Coronary heart disease?
• Breast cancer.
• Colon cancer.
• Ovarian cancer.
Examples of screening to identify individuals with a genetic predisposition to a disease

Screening for familial hypercholesterolemia (FH)

Identification of heterozygous carriers of FH (at increased risk of premature coronary artery disease)

Control of environmental factors e.g. cigarette smoking, diet and exercise

Prevention or delayed development of CAD
Prenatal Screening
Prenatal Screening in High Risk Group

To identify affected fetus

Termination of pregnancy
Before 120th day
Acceptability of termination?

- Genetic counselling to prepare the couple psychologically.
- Preparation for adequate management and care of affected child.
“Multiple Markers Screening”

Screening for a genetic disease using two or more markers

e.g. Triple test* for Down Syndrome in pregnant females

*The American College of Medical Genetics recommend that the triple test should be offered to all pregnant women
Neonatal Screening
Neonatal screening for identification of neonates with a genetic disease

Screening in new borns

Recognition of affected newborn

Dietary restriction or appropriate management

Prevention of severe clinical presentation
Examples of screening for identification of neonates with a genetic disease

- Phenylketonuria screening in newborns
- Recognition of PKU in newborns
- Dietary restriction of Phenylalanine
- Prevention of severe mental retardation and other clinical manifestations.
Newborn screening for treatable and/or preventable diseases

In several countries newborn screening is carried out for:

- Phenylketonuria.
- Congenital hypothyroidism.
- Sickle cell disease.
- Congenital adrenal hyperplasia.
- Galactosemia.
- Biotinidase deficiency.
- Maple syrup urine disease.
Genetic Counseling
Genetic Counselling

A educational process by which patients or at risk individuals are given information to understand the nature of the genetic disease, its transmission and the options open to them in management and family planning.
Genetic counselling - an integral part of the management of patients and families with genetic disorders
Genetic Counselling

An essential component of health counselling

For control of diseases with partial or complete genetic aetiology

- Single gene disorders
- Chromosomal anomalies
- Multifactorial disorders
- Mitochondrial disorders
Essential Components of Genetic Counselling

- History and pedigree construction
- Clinical Examination
  - History findings
  - Clinical examination findings
  - Radiology findings
  - Laboratory parameter results
  - DNA studies results
  - Others
- Confirmatory diagnosis
- Calculation of recurrence risk
- Counseling
- Available options
- Follow-up
COMPONENTS OF GENETIC COUNSELLING TEAM FOR CONGENITAL MALFORMATION

- Clinical Geneticist
- Obstetric.Gynaecologist
- Neonatologist
- Pediatrician
- Internist
- Cytogeneticist
- Molecular biologist
- Laboratory technologist
- Radiologist
- Data Analyst

One or more of these specialists

Comprehensive Genetic Counselling
The Genetic Counselling Process

**Why?**
- Have affected child
- Are carriers
- Have genetic disease in family
- Have recurrent abortions
- High maternal/paternal age
- Exposed to a mutagen/teratoge
- Are consanguineous

**Beneficiaries**
Individual or couple seeking counselling

**Counselling elements**

**Reaching accurate diagnosis**
- Family history
- Physical/clinical examination
- Cytogenetic studies/radiology
- Laboratory/DNA analysis

**Estimation of recurrence risk**
- Family pedigree
- Applying various risk calculation methods:
  - Bayesian
  - Mendels

**Genetic counselling**
- Available options
- Risk calculations
- New developments, etc.
- Disease course
- Treatment availability

**Decision making**
- Knowledge of disease recurrence
  - Non-directive
  - Available options
  - Family pressure
  - Religious beliefs
  - Social status
  - Economic status
  - Community influence
FUTURE STRATEGIES FOR CONTROL OF GENETIC DISORDERS

- Determine the frequency and distribution of genetic disorders in the population.
- Construct data bases of genetic disorders.
- Establish care and counselling facilities.
- Establish programs for carrier detection.
- Provision of appropriate counselling.
- Increase awareness of the genetic defects.
- Better understanding of molecular pathology of genetic defects.
- Update information.
AN ESSENTIAL ELEMENT OF ALL CONTROL AND PREVENTION PROGRAMS IS: AWARENESS
AWARENESS PROGRAMS

Pre-requisite for Prevention Programs

- Public Lectures
- Article in Newspapers
- Radio, TV, Video documentation
- Doctor-patient meetings
- Publications:
  - Booklets
  - Pamphlets
  - Posters
- Inclusion Curriculæ