SERVICES RELATED TO GENETICS

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GENETIC TESTING

- Invasive testing:
  - Amniocentesis
  - Chorionic villus sampling (CVS)
  - Cordocentesis
  - Preimplatation genetic diagnosis
  - Fetoscopy
- Non-invasive testing:
  - Ultrasonography
  - Maternal serum AFP
  - Isolation of foetal cells from maternal circulation

GENE THERAPY

- Gene Therapy is a field of medicine in which the genes are introduced into the body to cure the diseases.
- It is the intracellular delivery of genes to generate a therapeutic effect by correcting an existing abnormality.

Gene therapy involves

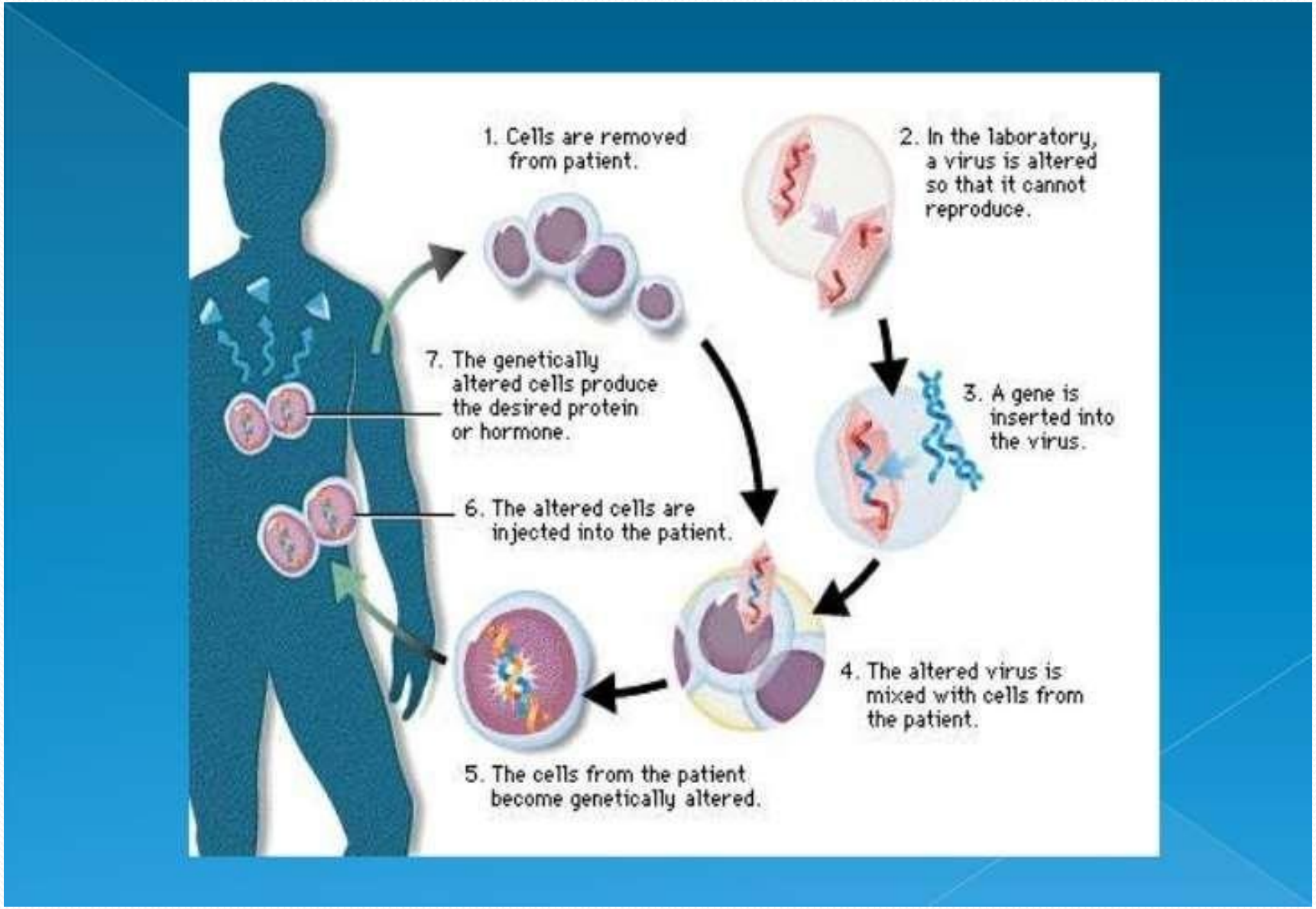
1. Detection of gene
2. Determination and its role
3. Isolation and cloning
4. Introducing the gene by proper way
   - germ line gene therapy
   -somatic gene therapy

Somatic cell gene therapy

- Somatic means non-productive cells of an organism
- These are the cells other than egg and sperm cells.

Ex: Bone marrow cells , blood cells , skin cells

- It involves the insertion of functional and expressible gene into a target somatic cell to correct the diseases permanently.


1. Cells are removed from patient.
2. In the laboratory, a virus is altered so that it cannot reproduce.
3. A gene is inserted into the virus.
4. The altered virus is mixed with cells from the patient.
5. The cells from the patient become genetically altered.
6. The altered cells are injected into the patient.
7. The genetically altered cells produce the desired protein or hormone.

Germ cell gene therapy

- Germ cells are reproductive cells.
- It involves introduction of DNA into germ cells, which is passed onto the next generations.
- Genetic alterations in somatic cells are not carried to next generations . Therefore somatic is preferred.

Cleaning Genes

One way germline therapy may be done to ensure a man with a genetic disease doesn't pass it to his child:

1 Doctors remove the man's sperm-producing cells, which contain a defective gene.

2 A healthy gene is added to each cell to replace the defective ones.

3 The cells are put into mouse testes.

4 They mature inside the mouse and start producing healthy human sperm.

5 Those sperm, once tested, are used to fertilize a woman's eggs in a laboratory dish.

6 The resulting embryos are placed in a woman's womb.

7 She gives birth to a child whose genes are free from the father's disease.

THE WASHINGTON POST

Approaches for gene therapy

1. Gene modification
   a)Replacement Therapy
   b)Corrective gene Therapy
2. Gene Transfer
   a)Physical(gene gun , naked DNA)
   b)Chemical($CaPO_4$ transfection)
   c)Biological(Viral vectors)
3. Gene transfer in special cell lines

- GENE GUN:

  Employs a high pressure delivery system to shoot tissue with gold or tungsten particles that are coated with DNA.

- MICROINJECTION:

  Process of using a glass micropipette to insert microscopic substances into a single living cell.

  Normally performed under a specialized optical microscopic setup called as micromanipulator.

- USING DETERGENTS:

  Certain charged chemical compounds like calcium phosphate are mixed with functional cDNA o desired function.

  The mixture is introduced at the vicinity of recipient cells.

  The chemicals disturb the cell membrane widens the pore size and allows the cDNA to pass through the cell.

- LIPOFECTION:

  It is a technique used to inject genetic material into a cell by means of liposomes.

  Liposomes are artificial phospholipid vesicles used to deliver a variety of molecules including DNA into the cells.

- Gene therapy is used to treat a number of diseases such as

  1. Cancer
  2. HIV
  3. Haemophilia
  4. Severe combined Immuno deficiencies
  5. Parkinson's disease
  6. Diabetes

TYPES OF GENE THERAPY

- **Ex vivo gene therapy**

  It involves transfer of genes into cultured cells which are then reintroduced into the patient.

  ex : bone marrow cells

- Technique involves following steps

1. Isolate cells with genetic defect
2. Grow the cells in culture
3. Introduce therapeutic gene to correct defect
4. Select genetically corrected genes and grow
5. Transplant the modified cells to the patient

- **In vivo gene therapy**

  Direct delivery of therapeutic gene into target cells of a particular tissue

  ex : liver , muscle ,skin , spleen.

1. Gene delivery by viral/non viral systems
2. By non viral systems means viral proteins induce inflammatory responses in host
3. Depends on efficiency of uptake of genes by target cells

VECTORS IN GENE THERAPY

- To transfer the desired gene into a target cell , a carrier is required.
- Such vehicles of gene delivery are known as vectors.
- Vectors are of two classes

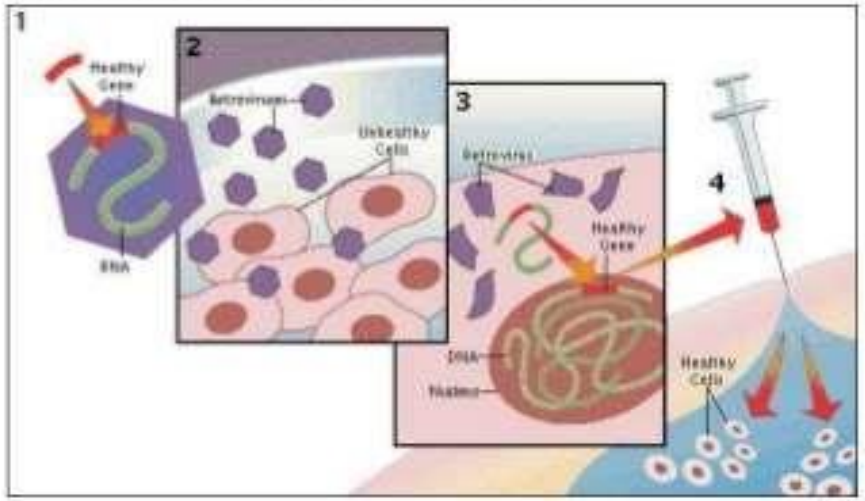
  1.Viral vectors

  2.Non-viral vectors

VIRAL VECTORS

1) RETROVIRUS VECTOR SYSTEM

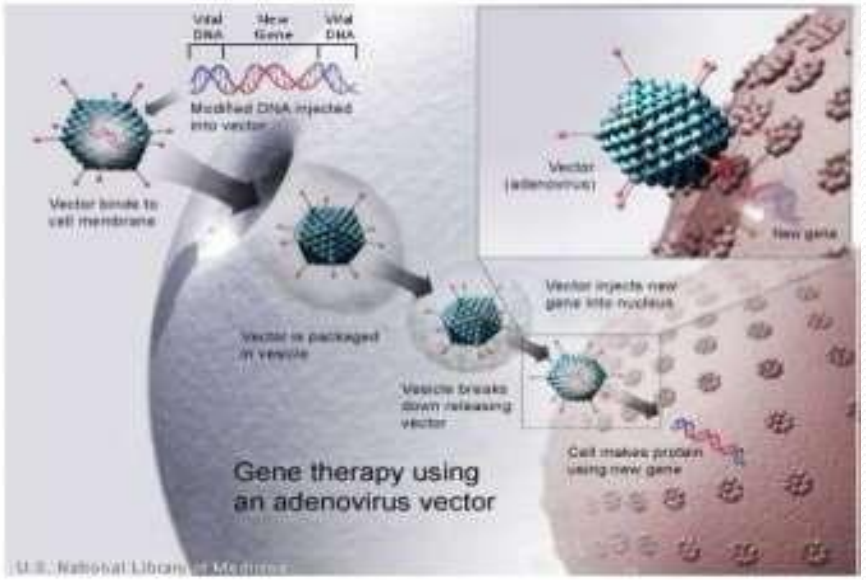
- The recombinant retroviruses have the ability to integrate into the host genome in a stable fashion.
- Can carry a DNA of size – **less than 3.4kb**
- Replication defective virus particles
- Target cell - dividing



VIRAL VECTORS

2) **ADENO VIRUS VECTOR SYSTEM**

- Adeno virus with a DNA genome – good vectors.
- Target- **non dividing human cell.**
- Eg. Common cold adenovirus.



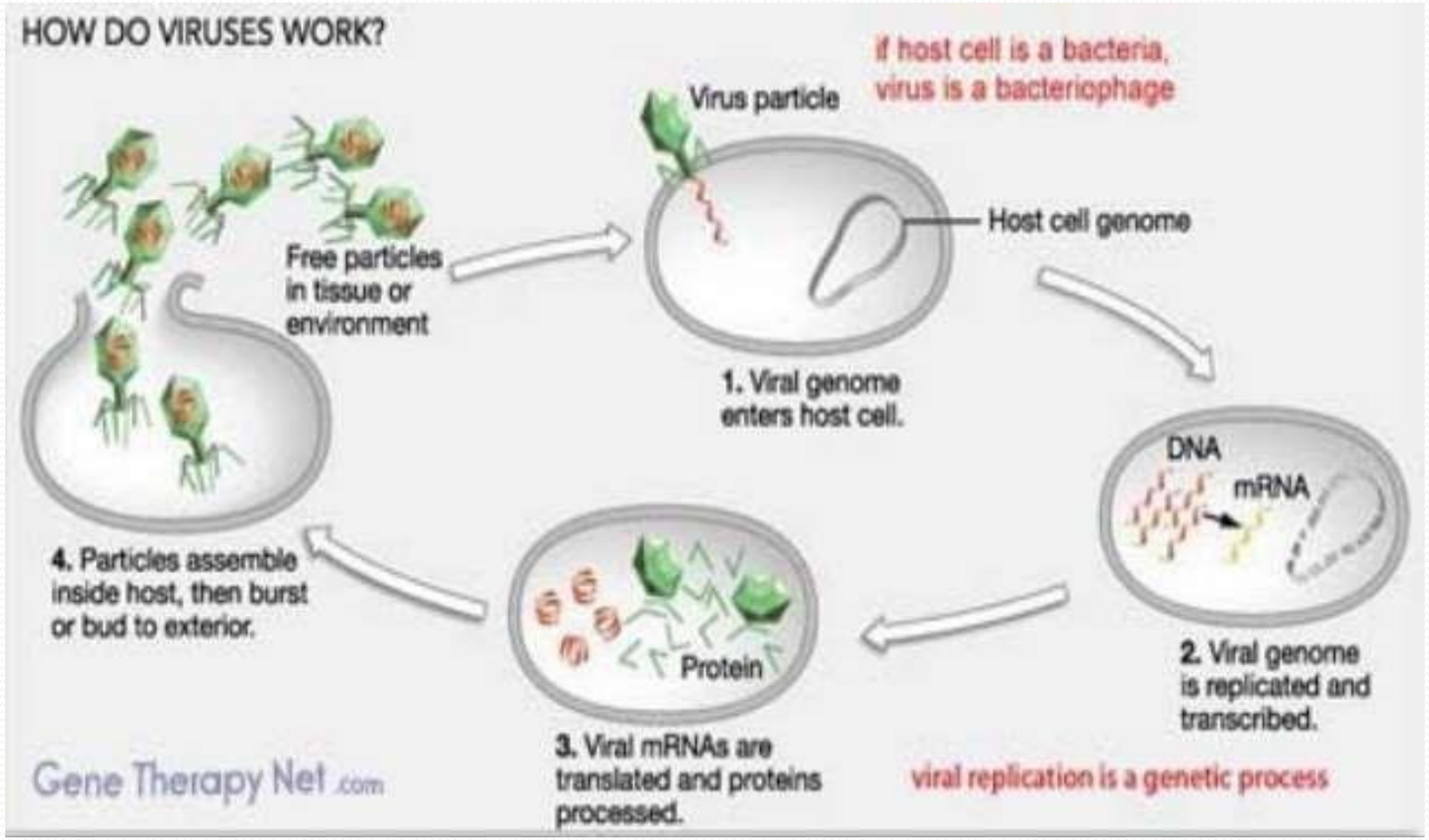
VIRAL VECTORS

3) ADENO ASSOCIATED VIRUS VECTOR

- It is a human virus that can integrate into chromosome 19.
- It is a single stranded, non pathogenic small DNA virus.
- AAV enters host cell, becomes double stranded and gets integrated into chromosome.

4) HERPEX SIMPLEX VIRUS VECTOR

- Viruses which have natural tendency to infect a particular type of cell.
- They infect and persist in **nervous cells.**


HOW DO VIRUSES WORK?
if host cell is a bacteria, virus is a bacteriophage
Virus particle
Host cell genome
Free particles in tissue or environment
1. Viral genome enters host cell.
DNA
mRNA
2. Viral genome is replicated and transcribed.
Protein
3. Viral mRNAs are translated and proteins processed.
4. Particles assemble inside host, then burst or bud to exterior.
Gene Therapy Net .com
viral replication is a genetic process

NON VIRAL VECTOR SYSTEM

1. **PURE DNA CONSTRUCT**

   - Direct introduction of pure DNA construct into target tissue .
   - Efficiency of DNA uptake by cells and expression rather low.
   - Consequently, large quantities of DNA have to be injected periodically.

2. **LIPOPLEXES**

   - Lipid DNA complexes; DNA construct surrounded by artificial lipid layer.
   - Most of it gets degraded by lysosomes.

NON VIRAL VECTORS

3) DNA MOLECULAR CONJUGATES

- Commonly used synthetic conjugate is poly- L- lysine bound to specific target cell receptor.
- Therapeutic DNA is then made to combine with the conjugate to form a complex.
- It avoids lysosomal breakdown of DNA.

4) HUMAN ARTIFICIAL CHROMOSOME

- Can carry a large DNA ie, with one or more therapeutic genes with regulatory elements.

GENETIC COUNCELLING

- The genetic is done by a genetic counselor who is a health professional who is academically and clinically prepared to provide genetic services to individuals and families seeking information about the occurrence, of risk of occurrence, of a genetic condition or birth defect.
- The counselor provides client-centered, supportive counseling regarding the issues, concerns, and experiences meaningful to the client's circumstances.

GENETIC COUNCELLING

- The genetic counselor communicates
  - **Genetic,**
  - **Medical and**
  - **Technical information**
- in a comprehensive, understandable manner with knowledge of psychosocial and cultural background of each client and their family.

Prenatal Genetic Counseling

- Preconception Counseling: if learned prior to conception that female and/or her partner are at high risk for having a child with a severe or fatal defect.
- Options will be:
  - Pre-implantation diagnosis - when eggs that have been fertilized in vitro (in a laboratory, outside of the womb) are tested for defects at the 8-cell (blastocyst) stage, and only non-affected blastocysts are implanted in the uterus to establish a pregnancy
  - Using donor sperm or donor eggs
  - Adoption

Indications for Prenatal Diagnosis

- Aadvanced maternal age
- Previous child with a chromosome abnormality
- Family history of a chromosome abnormality
- Family history of single gene disorder
- Family history of neural tube defect (NTD)

- Family history of other congenital structural abnormalities
- Abnormalities identified in pregnancy
- Other high risk factors (consanguinity, poor obstetric history, maternal illnesses)

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Process of Genetic Counselling

1) **Benificeries**: Individual or couple-

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

Process of Genetic Counselling

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

Process of Genetic Counselling

- 3) **Estimation of Recurrence Risk**-
- Family pedigree
- Applying various methods
- Risk calculation
- -Mendel's

Process of Genetic Counselling

- 4) **Genetic Counseling –**
- Available options
- Risk calculations
- New developments
- Disease course
- Treatment availability

Process of Genetic Counselling

- 5) **Decision making-**
- Knowledge of disease recurrence
- Available options
- Family pressure
- Religious beliefs
- Social status
- Economic status
- Community influence

ROLE OF A NURSE IN GENETIC COUNSELING

- Guiding a women or couple through prenatal diagnosis.
- Helping parents make decision in regard to abnormal prenatal diagnostic results.
- Assisting parents who have had a child with a birth defect to locate needed service and support.
- Providing support to help the family deal with the emotional impact of a birth defect.
- Coordinative services of other professionals, such as social workers, physical and occupational therapist, psychologist & dietician.

THANK YOU FOR YOUR ATTENTION….