



## ORGAN TRANSPLANTATION

### 65.1 INTRODUCTION

Transplantation is the process of taking a graft which may be a cell, tissue or an organ – from one site and placing it at another site in the same individual and or taking a graft – cell, tissue or organ from one individual – the donor and placing into another individual – the recipient. Graft can be Orthoptic i.e. the graft is placed at normal anatomical location of the organ (liver, heart) in the recipient or it can be Heterotopic i.e. the graft is located in different location (kidney, pancreas). Transplantation is required when a tissue or an organ either is congenitally non functional or becomes non functional due to injury or disease to restore the functions. The transplanted organ or tissue is known by the name of graft. Donor is the person who donates the tissue/organ to be grafted and recipient is the person who receives the tissue or the organ (graft). The earliest mention of patient's own skin grafted to correct the severed nose is in Sushruta Samhita (circa 800 BC).

First successful kidney transplant was an isograft, i.e. from the same species, same genetic make up (identical twins). Starzl in Denver performed the First liver transplant in 1963. Since then transplantation has developed a long way and now practically important different organs of the body are being transplanted to help patients. Donors can be cadaveric (after death) or live donors. We will discuss in brief the science and immunology of transplantation in this unit.



### OBJECTIVES

After reading this lesson, you will be able to:

- define transplantation
- describe the history of transplantation

- describe the various types of grafts
- describe the immunologic basis of allograft rejection
- discuss the classification and effector mechanisms of allograft rejection
- describe basics of prevention and treatment of allograft rejection
- define xenotransplantation.

### 65.2 HISTORY OF TRANSPLANTATION

The earliest mention of patient's own skin grafted to correct the severed nose is in Sushruta Samhita (circa 800 BC). Since then attempts have been made to somehow restore the functionality of diseased/deformed organs by transplanting tissues/organs from healthy donors. Many scientists working on various aspects of transplantation and succeeding in one or the other aspect have been awarded Nobel Prize. As mentioned above the kidney and liver transplantation was first attempted in 1960s.

The details of work done by of some of the Nobel Prize awardees on transplantation parameters are given below:

- Alexis Carrel (France) awarded Nobel Prize in Physiology or Medicine 1912 for his work on vascular suture and the transplantation of blood vessels and organs.
- Peter Brian Medawar awarded Nobel Prize in Physiology or Medicine 1960 for the Discovery of acquired immunological tolerance; that the graft reaction is an immunity phenomenon and in 1950s, induced immunological tolerance to skin allografts in mice by neonatal injection of allogeneic cells.
- Joseph E. Murray Joseph E. Murray awarded Nobel Prize in Physiology or Medicine 1980 and 1990 for his discoveries concerning organ transplantation in the treatment of human disease; in 1954, the first successful human kidney transplant was performed between twins in Boston; transplants were possible in unrelated people if drugs were taken to suppress the body's immune reaction Human transplantation antigens (HLA) ---- MHC.
- Gertrude B. Elion, George H. Hitchings were awarded Nobel Prize in Physiology or Medicine in 1988 for discoveries of important principles for drug treatment i.e. immunosuppressant drug (The first cytotoxic drugs) ---- azathioprine for preventing rejection of grafts.

Now a day's transplantation of organs is one of the mainstream subjects of medicine and many people are being helped by transplantation. Almost any one of the important organs can be transplanted. Transplantation is much advanced now. Today, kidney, pancreas, heart, lung, liver, bone marrow, and cornea transplantations are performed among non-identical individuals with ever increasing frequency and success.





Notes



**INTEXT QUESTIONS 65.1**

1. ....is the process of taking a graft from donor to recipient
2. Graft placed at normal anatomical location of the organ is called .....
3. Graft located in different location is called .....
4. The transplanted organ or tissue is called as .....

**65.3 DEFINITION OF TERMS USED IN TRANSPLANTATION**

You may not be familiar with the terms used in transplantation science. These are explained below.

**Autograft:** cell tissue taken from one site of body and transplanted to the damaged site. Best example is skin grafting in a burns case.

**Isograft:** it is the term used when tissue/organ taken from one member of the species is transplanted in another member of the same genetic makeup (syngeneic) of the same species. Examples are liver, kidney transplantation done between identical twins.

**Allograft:** it is the term used when tissue/organ taken from one member of the species is transplanted in another member of the same species. There will be genetic differences between recipient and donor.

**Xenograft:** Tissue or organ taken from one species is transplanted in another species.

**Donor:** Person who donates the organ or tissue.

**Recipient:** Person who receives the tissue or organ from the donor.

**MHC:** Major histocompatibility complex.

**HLA:** Histocompatibility locus antigens

**65.4 CLASSIFICATION OF GRAFTS**

Grafts are classified according to the site, species and type of donor involved in transplantation. Briefly it is described below.

**65.4.1 According to species**

- Autologous grafts also known as autografts:

Grafts transplanted from one part of the body to another in the same individual

- Syngeneic grafts also known as isografts:

Grafts transplanted between two genetically identical individuals of the same species, e.g. between identical twins

- Allogeneic grafts also known as allografts:

Grafts transplanted between two genetically different individuals of the same species e.g. kidney from son to father, etc.

- Xenogeneic grafts also known as xenografts:

Grafts transplanted between individuals e.g. organ from an animal species transplanted in another species.



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### 65.4.2 According to site of grafting:

- Orthotopic:

Graft at normal anatomical location of the organ (liver, heart)

- Heterotopic:

Graft located in different location (kidney, pancreas)

### 65.4.3 According to source of graft:

- Live donor graft

The graft is from a living matched donor.

- Cadaveric (after death) donor graft

The graft is from a donor who has died due to some sickness, accident, etc.

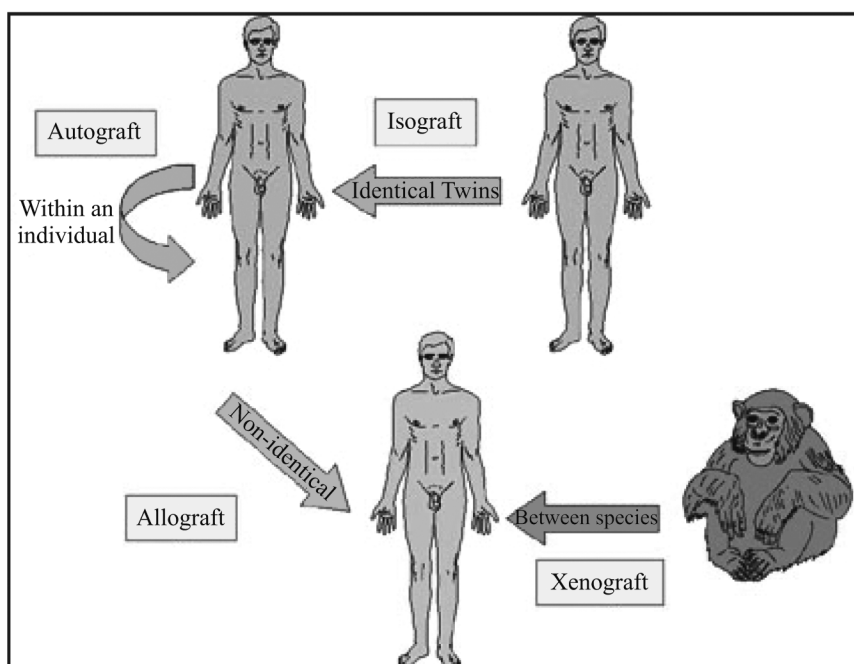


Fig. 65.1: Types of grafts according to species



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**INTEXT QUESTIONS 65.2**

Match the following:

- |              |  |
|--------------|--|
| 1. Autograft | a. Grafts transplanted between two genetically different individuals of the same species |
| 2. Allograft | b. Grafts transplanted between two genetically identical individuals                     |
| 3. Xenograft | c. Grafts transplanted from one part of the body to another in the same individual       |
| 4. Isograft  | d. Grafts transplanted from dead donor   |
| 5. Cadaver   | e. Grafts transplanted from one species to another species                               |

### 65.5 IMMUNOLOGIC BASIS OF ALLOGRAFT REJECTION

In earlier days when there was no understanding about transplantation, one of the major problems in transplantation was the rejection of the graft. Gradually after studies it was found that the grafts rejection is a kind of specific immune response to the antigens in the grafted organ/tissue. The phenomenon was specific and imparted immune memory in the recipient of graft if the graft from the same donor was transplanted again the recipient will reject the graft faster compared to first time. This was due to the immune memory of the first graft.

Grafts rejection can be of two types:

- First set rejection
- Second set rejection

#### 65.5.1 First set rejection:

In initial set of experiments in experimental animals the skin graft was transplanted from one animal to another animal of the same species. The graft appeared to be accepted initially as it was vascularised and was normal morphologically and functionally. However it was seen that by fourth day the graft was invaded by lymphocytes, it was inflamed, blood vessels were occluded by thrombi, ischemia (decreased vascularity) and necrosis (death of graft tissue) set in and graft became shrunken looking like a scab and sloughed off by 10th day. This is first set rejection.

### 65.5.2 Second set rejection:

A second graft transplanted from same donor in the same recipient results in accelerated rejection. The same set of events as described above happens but at an accelerated rate and graft is rejected by 6th day.

## 65.6 IMMUNOLOGIC BASIS OF GRAFT REJECTION

Transplantation antigens are the antigens which need to be taken into consideration for both the donor and the recipient to ensure successful transplantation. These include Major histocompatibility antigens (MHC molecules), Minor histocompatibility antigens (HLA antigens) and other alloantigens (ABO blood group, and some tissue specific antigens, etc.). Mismatch of these antigens in donor and recipient is a strong factor for graft rejection.

### 65.6.1 Mechanism of allograft rejection

- Cell-mediated Immunity: Recipient's T cell-mediated cellular immune response against alloantigens on grafts (recognize the allogeneic MHC molecules as foreign) lead to graft rejection.
- Humoral Immunity: Complements activation, antibody dependent cell cytotoxicity, opsonization, etc. This is brought about by enhancing and blocking antibody which results in hyperacute rejection of graft.
- Role of NK cells: NK cells get activated and help in graft rejection.

## 65.7 EFFECTOR MECHANISMS OF ALLOGRAFT REJECTION

Allograft rejection can be of two types:

Host versus graft reaction (HVGR)

Graft versus host reaction/disease (GVHR/GVHD)

### 65.7.1 Host versus graft reaction (HVGR)

The host rejects the graft as seen in conventional organ transplantation. This may be due to mismatch of MHC and other alloantigens. HVGR can be Hyperacute rejection (occurs within minutes of transplantation), acute rejection (occurs within days to 2 weeks after transplantation, 80-90% of cases occur within 1 month) and chronic rejection (develops months or years after acute rejection reactions have subsided). Antibody against ABO blood type antigen; antibody against VEC antigen and antibody against HLA antigen, either preformed or formed after the graft due to mismatch/partial match is the basic cause of rejection of graft.



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### 65.7.2 Graft versus host reaction/disease (GVHR/GVHD):

Here the graft is immunologically more powerful and so kind of starts reaction against the host. Examples are bone marrow transplantation and immune cells transplantation. In graft versus host disease (GVHD) the immunocompetent cells in the graft react against the minor histocompatibility antigens and other antigens which can damage the host.

## 65.8 PREVENTION AND TREATMENT OF ALLOGRAFT REJECTION

Detailed laboratory work is extremely important that will ensure that the donor and recipient match genetically and this will help to minimize the graft rejection. The tests include tissue typing. The other modalities to minimize graft rejection are immunosuppressive therapy and induction of immune tolerance.

### 65.8.1 Tissue typing includes:

- ABO and Rh blood typing
- Crossmatching (Preformed antibodies)
- HLA typing
  - HLA-A and HLA-B
  - HLA-DR

### 65.8.2 Immunosuppressive therapy

Various drugs are given to suppress the immune response of the host. These include:

- Cyclosporine
- Azathioprine, Cyclophosphamide
- Ab against T cell surface molecules
- Anti-inflammatory agents like corticosteroids, etc.

### 65.8.3 Induction of immune tolerance by:

- inhibition of T cell activation by injecting soluble MHC molecules in the recipient
- administration of anti-IL2R mAb
- administration of Th2 cytokines like anti-TNF- $\alpha$ , anti-IL-2, anti-IFN- $\gamma$  mAb

## 65.9 XENOTRANSPLANTATION

The demand for transplantation of organs damaged due to various diseases is increasing day by day. The availability of organs is a big issue. Various scientists

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are trying to transplant organs from animal species in the humans (experimental stage). Such grafts are called xenografts. So xenotransplantation is defined as the transplantation of organ from one species to another species e. g. pig heart in a human being and so on. So far there has been no success.



### INTEXT QUESTIONS 65.3

1. ...., ..... & ..... antigens are factors for graft rejection
2. Types of graft rejection are ..... & .....
3. Types of Allograft rejection are ..... & .....
4. Transplanting organs from animal species to human is known as .....



### WHAT YOU HAVE LEARNT

- Transplantation is the process of taking a graft which may be a cell, tissue or organs – from one site and placing it at another site in the same individual and or taking a graft – cell, tissue or organs from one individual – the donor and placing into another individual – the recipient. Transplantation is required when a tissue or an organ either is congenitally non functional or becomes non functional due to injury or disease to restore the functions. The earliest mention of patient's own skin grafted to correct the severed nose is in Sushruta Samhita (circa 800 BC).
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- Now a day's transplantation of organs is one of the mainstream subjects of medicine and many people are being helped by transplantation.
- Grafts are classified according to the site, species and type of donor involved in transplantation. According to species can be autografts: grafts transplanted from one part of the body to another in the same individual; isografts: grafts transplanted between two genetically identical individuals of the same

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Microbiology



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species, e.g. between identical twins; allografts: grafts transplanted between two genetically different individuals of the same species e. g. kidney from son to father, etc. xenografts: grafts transplanted between individuals e. g. organ from an animal species transplanted in another species; on basis of site of grafting: orthotopic: graft at normal anatomical location and heterotopic: graft located in different location and finally according to source of graft: live donor graft: the graft is from a living matched donor and

- Grafts rejection can be of two types:

First set rejection

Second set rejection

- Transplanted graft maybe rejected that is due to the immunological mechanism. Transplantation antigens are the antigens which need to be taken into consideration for both the donor and the recipient to ensure successful transplantation. These include Major histocompatibility antigens (MHC molecules), Minor histocompatibility antigens (HLA antigens) and other alloantigens (ABO blood group, and some tissue specific antigens, etc.). Mismatch of these antigens in donor and recipient is a strong factor for graft rejection. Cell-mediated Immunity, humoral immunity and NK cells play a role in graft rejection.
- Detailed laboratory work is extremely important that will ensure that the donor and recipient match genetically and this will help to minimize the graft rejection. The tests include tissue typing. The other modalities to minimize graft rejection are immunosuppressive therapy and induction of immune tolerance.



## ANSWERS TO INTEXT QUESTIONS

### 65.1

1. Transplantation
2. Orthoptic
3. Heterotopic
4. Graft

### 65.2

1. (c)
2. (a)

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3. (e)
4. (b)
5. (d)

### 65.3

1. Major Histocompatibility antigens, minor histocompatibility antigens and alloantigens
2. First set & second set rejection
3. Host versus graft reaction and Graft versus Host reaction/disease
4. Xenotransplantation

## MODULE

Microbiology



Notes

