BHARATHIDASAN UNIVERSITY

Tiruchirappalli- 620024,
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Programme: M.Sc., Biomedical Science

Course Code: BM35C6
Course Title: Immunology

Unit-V
Overview of Autoimmunity and Transplantation

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Unit V:

- Overview of Autoimmunity and Transplantation - Autoimmune disease – Spectrum – organ specific (thyroid diseases, IDDM, pernicious anemia) and non-organ specific (Systemic sclerosis & SLE). Factors governing autoimmune diseases- genetic, hormonal, microbial and non-microbial. Regulatory mechanisms involved in autoimmune diseases- Tolerance – breakdown of tolerance (Modification of auto antigen, Cross-reactions with B cell epitopes, molecular mimicry of T cell epitopes. Transplants –auto, allo and Xeno- immunological complications of transplantation – graft rejection, GVHD –mechanisms – prevention of graft rejection- Immunosuppressant Drugs (Glucocorticoids, Calcineurin inhibitors, Antiproliferative/Antimetabolic agents) and antibodies as immunosuppressant

PRESENTATION: 3

TRANSPLANTS AND ITS TYPES

Introduction to Organ Transplantation

- **Definition** :

Organ transplantation is a surgical procedure of transferring an organ from one body (donor) to another (recipient) to replace a failing or damaged organ.

- **Importance of immunology** :

The immune system plays a central role in determining the success of a transplants .understanding how the immune system responds to foreign tissue is crucial for preventing rejection and ensuring long-term graft survival.

Types of Transplants

- **AUTOGRAFTS** :

  Transplant of tissue within the same individual(e. g. skin grafts).

- **ALLOGRAFTS** :

  Transplant from a donor to a genetically different individual of the same species (most common in humans).

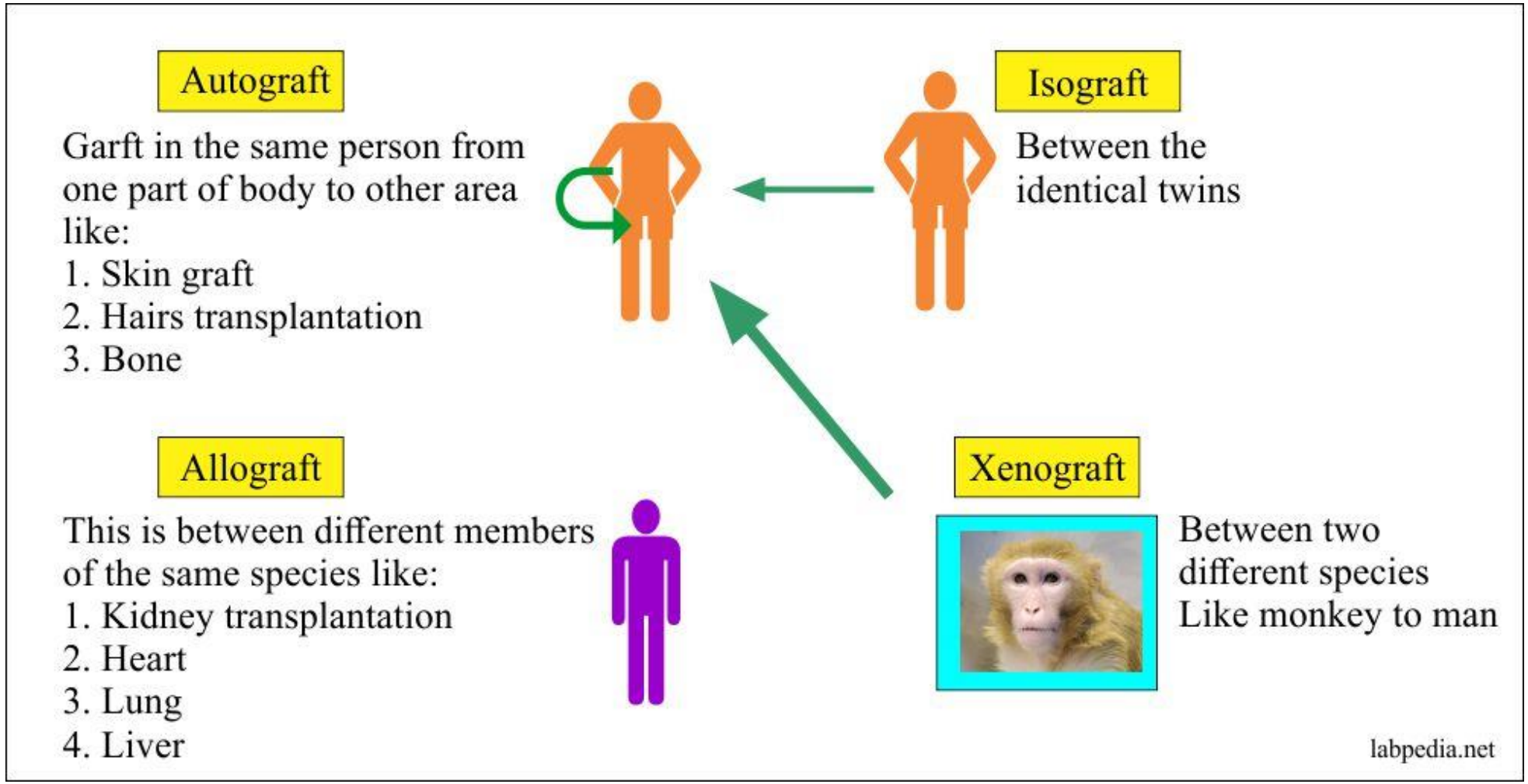
- **XENOGRAFTS** :

  Transplant between different species (e.g.,pig heart valves).

- **ISOGRAFTS** :

  Transplant between genetically identical individuals (e.g.,identical twins).

Types of Transplants



AUTOGRAFT :

An autograft is a transplant of tissue from one part of the body to another within the same individual. Since the tissue is the patient's own, there's no risk of rejection by the immune system.

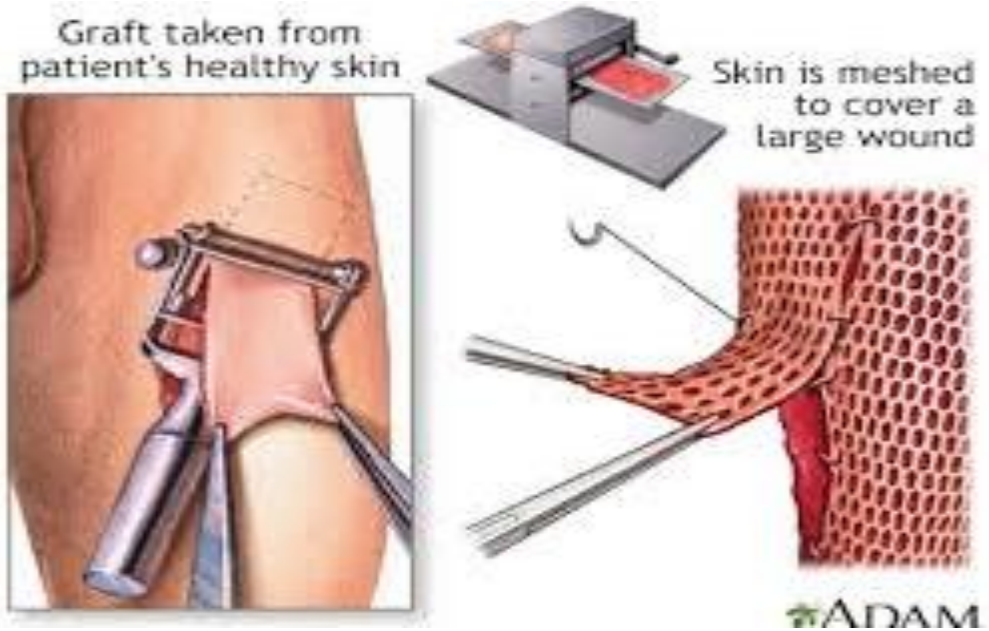
Examples:

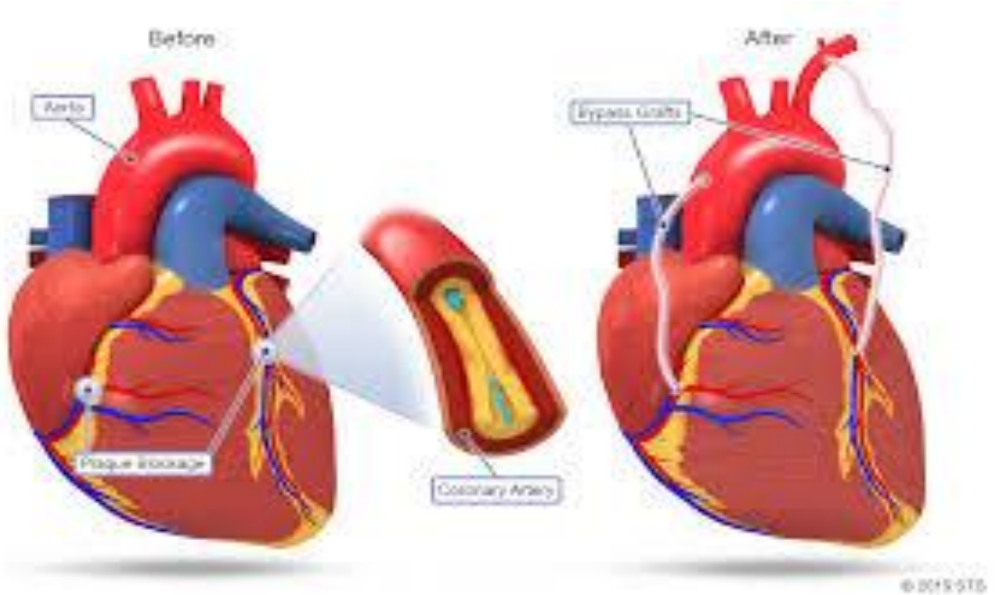
Skin grafts for burn victims: Skin is taken from an unaffected area of the body and transplanted to the damaged area.

Coronary artery bypass surgery: A blood vessel from the leg (typically the saphenous vein) is used to bypass blocked arteries in the heart.

Immunological Aspect: No immune response is triggered since the tissue is genetically identical to the host

AUTOGRAFT


Graft taken from patient's healthy skin
Skin is meshed to cover a large wound
A.D.A.M.


Before
After
Aorta
Bypass Grafts
Plaque Blockage
Coronary Artery

ALLOGRAFT :

Definition:

An allograft involves transplanting an organ or tissue from one individual to another of the same species but with different genetic makeup (most common in human organ transplants).

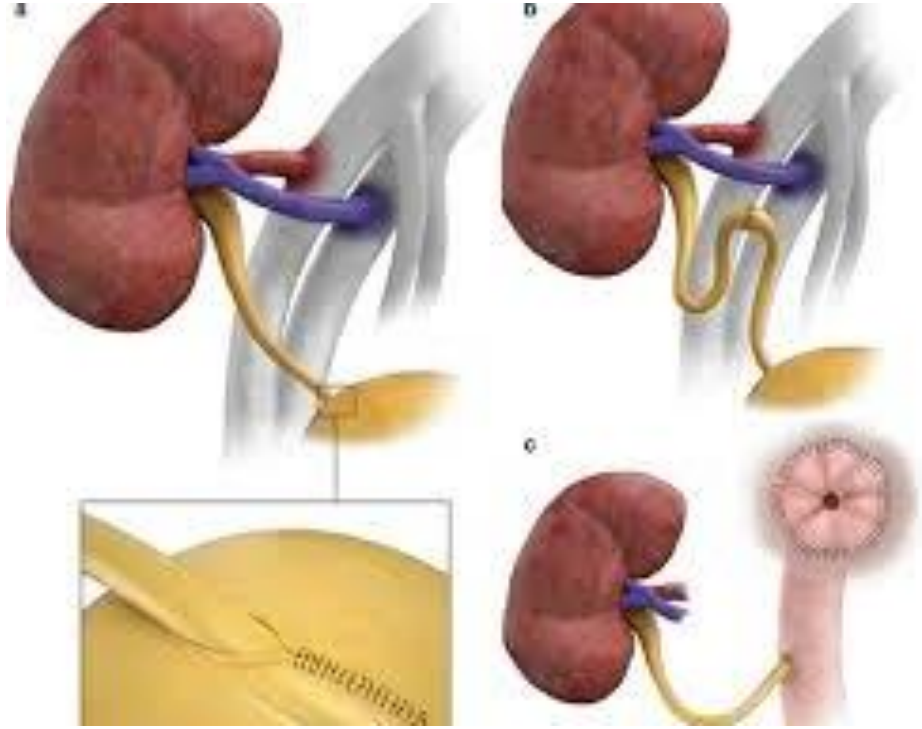
Examples:

Kidney transplant: One of the most common types of transplants, where a kidney is transplanted from a living or deceased donor to a recipient with kidney failure.

Liver transplant: Used to treat end-stage liver disease or liver failure.Heart transplant: For patients with end-stage heart failure, replacing the damaged heart with a healthy one from a donor.

Immunological Aspect: Since the donor organ is foreign, the recipient's immune system recognizes it as non-self, triggering an immune response. This requires careful HLA matching and long-term immunosuppressive therapy to prevent rejection.

ALLOGRAFT



XENOGRAFT:

Definition:

A xenograft is a transplant from one species to another. This type of transplant is much more complex due to the significant genetic differences between species.

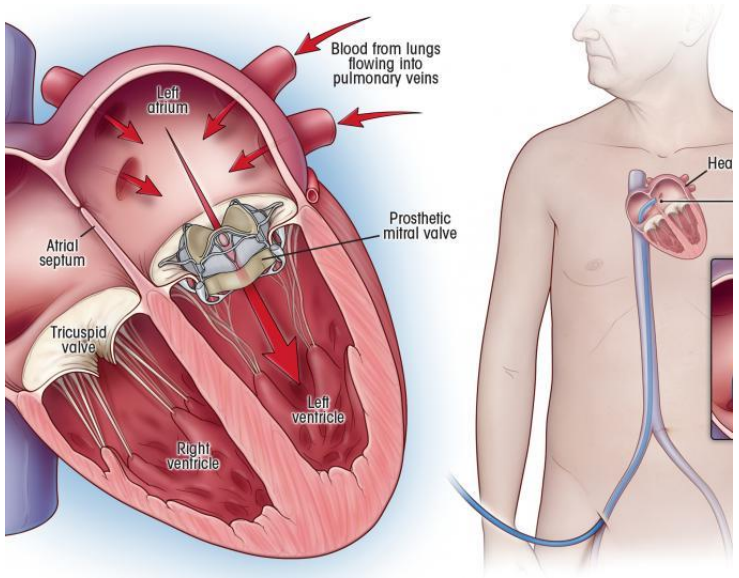
Examples:

Heart valve replacement: Often, heart valves from pigs or cows are used in human patients. These valves are treated and modified to reduce immune response.

Experimental xenotransplants: Research is ongoing to use genetically modified pig organs (such as kidneys and hearts) in humans to address organ shortages.

Immunological Aspect: Xenografts pose a high risk of rejection because of the vast differences in antigens between species. Despite genetic modification and immunosuppressive drugs, the recipient's immune system often recognizes the organ as highly foreign. This area of transplantation is still under experimental investigation.

XENOGRAFT


Blood from lungs flowing into pulmonary veins
Left atrium
Prosthetic mitral valve
Atrial septum
Tricuspid valve
Left ventricle
Right ventricle


POTENTIAL USES FOR XENOTRANSPLANTATION PRODUCTS
PIG SKIN FOR BURNS
DONOR PIG
PIG PANCREATIC ISLETS FOR DIABETES
HUMAN RECIPIENT

THE IMMUNE RESPONSE TO TRANSPLANTS

Foreign Antigens:

- The immune system recognizes the transplanted organ as foreign due to differences in surface molecules, primarily Human Leukocyte Antigens (HLAs) or Major Histocompatibility Complex (MHC) molecules.

  MHC Class I & II:

  > Present on the surface of donor cells, triggering the recipient's immune response.

Role of T-Cells:

- Helper T-Cells (CD4+): Recognize foreign MHC molecules and activate other immune cells.
- Cytotoxic T-Cells (CD8+): Attack the donor cells directly, leading to graft rejection.

TYPES OF TRANSPLANT REJECTION :

1. Hyperacute Rejection:

- Occurs within minutes to hours after transplantation.
- Caused by pre-existing antibodies in the recipient that target donor antigens (e.g., ABO blood group incompatibility).
- Prevention: Cross-matching donor and recipient blood for compatibility.

2. Acute Rejection:

- Occurs days to weeks post-transplant.
- Mediated primarily by T-cells that recognize the foreign MHC molecules.
- Characterized by inflammation and tissue damage in the graft.
- Managed with immunosuppressive drugs.

3. Chronic Rejection:

- Develops over months to years.
- Results from long-term immune response, leading to fibrosis and gradual loss of organ function.
- Difficult to treat and remains a major challenge in transplantation.

IMMUNOSUPPRESSION IN TRANSPLANTATION

Immunosuppressive Drugs:

- Medications used to prevent the immune system from attacking the transplanted organ.
- Calcineurin Inhibitors (e.g., Cyclosporine, Tacrolimus): Suppress T-cell activation.
- Corticosteroids:Reduce overall immune activity and inflammation.
- Antiproliferative Agents (e.g., Mycophenolate Mofetil): Inhibit proliferation of immune cells.

Goal:

Achieve a balance between preventing rejection and maintaining sufficient immune activity to fight infections and cancer.

Graft-Versus-Host Disease (GVHD)

Definition:

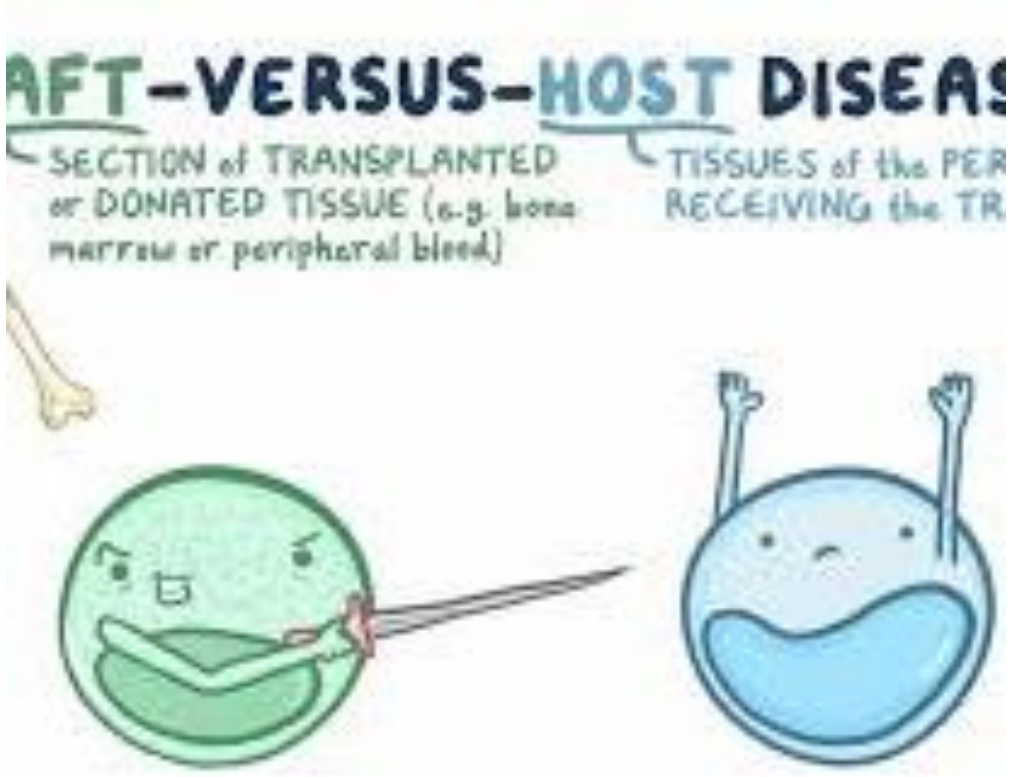
- Occurs when immune cells from the transplanted tissue (usually bone marrow or stem cells) attack the recipient's tissues.

Mechanism:

- Donor T-cells recognize the recipient’s cells as foreign and initiate an immune response.

Prevention:

- Immunosuppressive therapy to reduce the activity of donor T-cells.



Future of Immunology in Transplantation

Biomarkers:

- Identifying immune biomarkers that predict rejection can lead to personalized immunosuppressive therapy.

Stem Cell Transplantation:

- Using stem cells to regenerate damaged tissues or organs, reducing the need for whole-organ transplants.

Xenotransplantation:

- Research is underway to make animal organ transplants (e.g., from genetically modified pigs) viable, potentially addressing organ shortages.

KEYPOINTS :

- Transplantation is the process of moving cells, tissues or organs from one site to another for the purpose of replacing or repairing damaged or diseased organ and tissues.
- It saves thousands of lives each year. However , the immune system poses a significant barrier to successful organ transplantation when tissues/organ are transferred from one individual to another.
- Rejection is caused by the immune system identifying the transplant as foreign, triggering a response that will ultimately destroy the transplanted organ or tissue.
- Long term survival of the transplant can be maintained by manipulating the immune system to reduce the risk of carefully .

- Donor and recipient are carefully matched prior to transplantation to minimize the risk of rejection. They are matched based on their blood group, tissue and how the recipient’s blood serum reacts to donor cells.
- Immunosuppressive drugs are used to prevent and treat transplant rejection by dampening the overall immune response. However , immunosuppressive drugs are non–specific and leave patients more susceptible to disease.

Conclusion :

- Immunology plays a vital role in the success of organ transplantation.
- Preventing rejection through a combination of HLA matching and immunosuppressive therapies is essential.
- Advances in understanding immune tolerance and developing innovative therapies hold great promise for improving outcomes in transplant recipients.

RECENT IMPROVEMENTS IN TRANSPLANTATION :

- **Better Organ Preservation:** Enhanced techniques like normothermic machine perfusion improve the viability of organs for transplant.

- **More Living Donor Transplants**: Increased use of living donors, especially for kidneys and livers, due to better surgical techniques and outcomes.

- **Personalized Medicine:** Customized immunosuppressive therapies based on genetic profiles to improve transplant success and reduce side effects.

- **Advances in Bioengineering:** Development of lab-grown organs and 3D-printed tissues to address organ shortages.

- **Improved Policies:** Enhanced practices and policies to ensure fairer organ distribution and reduce waiting times.

ACKNOWLEDGEMENT

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