SUB. NAME: ARTIFICIAL ORGANS AND TISSUE ENGINEERING UNIT III SUB.CODE: SBM1306

TRANSPLANTATION: 1. Transplantation types, 2. Immunological considerations, 3. Blood transfusion. 4. Individual organs- 4.1kidney, 4.2 liver, 4.3 heart & lung, 4.4 bone, 4.5 skin, 4.6 hair , 4.7 pancreas 5. Regeneration

1. Transplantation types

1.1Autograft

Autografts are the transplant of tissue to the same person. Sometimes this is done with surplus tissue, tissue that can regenerate, or tissues more desperately needed elsewhere (examples include skin grafts, vein extraction for CABG, etc.). Sometimes an autograft is done to remove the tissue and then treat it or the person before returning it (examples include stem cell autograft and storing blood in advance of surgery).

1.2Allograft and allotransplantation

An allograft is a transplant of an organ or tissue between two genetically non-identical members of the same species. Most human tissue and organ transplants are allografts. Due to the genetic difference between the organ and the recipient, the recipient's immune system will identify the organ as foreign and attempt to destroy it, causing transplant rejection.

1.3Isograft

A subset of allografts in which organs or tissues are transplanted from a donor to a genetically identical recipient (such as an identical twin). Isografts are differentiated from other types of transplants because while they are anatomically identical to allografts, they do not trigger an immune response.

1.4 Xenograft and xenotransplantation

A transplant of organs or tissue from one species to another. An example is porcine heart valve transplant, which is quite common and successful. Another example is attempted piscine-primate (fish to non-human primate) transplant of islet (i.e. pancreatic or insular tissue) tissue. The latter research study was intended to pave the way for potential human use if successful. However, xenotransplantion is often an extremely dangerous type of transplant because of the increased risk of non-compatibility, rejection, and disease carried in the tissue.

Success of transplantation between identical twins proposes that the success rate depends on the amount of sharing of histo compatibility genes.

Histocompatibility genes are responsible for the production of antigens on cell surface. With reference to the surface antigens, the grafts or transplants are differentiated in to four types.

They are as follows:

1. Auto graft or Autogenic graft

2. Isograft or Syngraft or Syngenetic graft,

3. allografts or Homografts,

4. Xenograft.

1. Auto graft or Autogenic graft:

When tissue is transplanted from one site to another in the same individual, the transplant is referred as "auto graft" or "autogenic graft" (From Greek Auto=Self).

Immune system of recipient accepts the auto graft very easily, because antigens of recipient cells and the transplanted tissue are alike.

2. Isograft or Syngraft or Syngentic graft:

The graft taken from a genetically identical person is known as Isograft or Syngraft or Syngentic graft. This kind of transplantation is possible between two genetically identical twins.

Since development of identical twins takes place from a single zygote, identical twins share same genes that are responsible for the production of antigens.

3. Allograft or Homograft:

If the transplantation is carried between genetically different members of the same species then graft is called as "allograft". The allograft is formally named as "Homograft".

The histo compartbility antigens of allograft are dissimilar with the host histo compartbility antigens. Hence immune system of recipient/ host identifies the graft as foreign and induces an immune response against to it, resulting rejection of graft.

4. Xenograft:

If the transplantation between individuals of two different species is carried, for eg. Transplanting monkey liver to human, the graft is referred as "Xenograft".

Since the histocompatibility genes are quite different, hosts body rejects the graft more vigorously.

3. Blood transfusion

Blood transfusion is generally the process of receiving blood or blood products into one's circulation intravenously. Transfusions are used for various medical conditions to replace lost components of the blood. Early transfusions used whole blood, but modern medical practice commonly uses only components of the blood, such as red blood cells, white blood cells, plasma, clotting factors, and platelets.

Red blood cell transfusion was considered when the hemoglobin level fell below 10 g/dL or hematocrit falls below 30% (the "10/30 rule"). Because each unit of blood given carries risks, a trigger level lower than that at 7–8 g/dL is now usually used as it has been shown to have better patient outcomes. The administration of a single unit of blood is the standard for hospitalized people who are not bleeding, with this treatment then followed with re-assessment and consideration of symptoms and hemoglobin concentration. Patients with poor oxygen saturation may need more blood. The advisory caution to use blood transfusion only with more severe anemia is in part due to evidence that outcomes are worsened if larger amounts are given. One may consider transfusion for people with symptoms of cardiovascular disease such as chest pain or shortness of breath. In cases where patients have low levels of hemoglobin but are cardiovascularly stable, parenteral iron is a preferred option based on both efficacy and safety

Blood transfusions typically use sources of blood: one's own (autologous transfusion), or someone else's (allogeneic or homologous transfusion). The latter is much more common than the former. Using another's blood must first start with donation of blood. Blood is most commonly donated as whole blood intravenously and collecting it with an anticoagulant. In developed countries, donations are usually anonymous to the recipient, but products in a blood bank are always individually traceable through the whole cycle of donation, testing, separation into components, storage, and administration to the recipient. This enables management and investigation of any suspected transfusion related disease transmission or transfusion reaction.

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Procedure

Before a blood transfusion is given, there are many steps taken to ensure quality of the blood products, compatibility, and safety to the recipient. In 2012, a national blood policy was in place in 70% of countries and 62% of countries had specific legislation that covers the safety and quality of blood transfusion.

Blood donation

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In developing countries the donor is sometimes specifically recruited by or for the recipient, typically a family member, and the donation occurs immediately before the transfusion.

Processing and Testing

Donated blood is usually subjected to processing after it is collected, to make it suitable for use in specific patient populations. Collected blood is then separated into blood components by centrifugation: red blood cells, plasma, platelets, albumin protein, clotting factor concentrates, cryoprecipitate, fibrinogen concentrate, and immunoglobulins (antibodies). Red cells, plasma and platelets can also be donated individually via a more complex process called apheresis.

- All donated blood is tested for infections. The current protocol tests donated blood for HIV-1, HIV-2, HTLV-1, HTLV-2, Hepatitis B, Hepatitis C, Syphilis (*Treponema pallidum*),. In addition, platelet products are also tested for bacterial infections due to its higher inclination for contamination due to storage at room temperature..
- All donated blood is also tested for ABO and Rh groups, along with the presence of any red blood cell antibodies.
- Pathogen Reduction treatment that involves, for example, the addition of riboflavin with subsequent exposure to UV light has been shown to be effective in inactivating pathogens (viruses, bacteria, parasites and white blood cells) in blood products. By inactivating white blood cells in donated blood products, riboflavin and UV light treatment can also replace gamma-irradiation as a method to prevent graft-versus-host disease (TA-GvHD).

Compatibility testing

Before a recipient receives a transfusion, compatibility testing between donor and recipient blood must be done. The first step before a transfusion is given is to Type and Screen the recipient's blood. Typing of recipient's blood determines the ABO and Rh status. The sample is then Screened for any alloantibodies that may react with donor blood. It takes about 45 minutes to complete (depending on the method used). The blood bank scientist also checks for special requirements of the patient (e.g. need for washed, irradiated or CMV negative blood) and the history of the patient to see if they have a previously identified antibodies and any other serological anomalies.

Adverse effects

In the same way that the safety of pharmaceutical products are overseen by pharmacovigalence, the safety of blood and blood products are overseen by Haemovigilance. This is defined by the World Health Organization (WHO) as a system "...to identify and prevent occurrence or recurrence of transfusion related unwanted events, to increase the safety, efficacy and efficiency of blood transfusion, covering all activities of the transfusion chain from donor to recipient." The system should include monitoring, identification, reporting, investigation and analysis of adverse events near-misses and reactions related to transfusion and manufacturing.

Transfusions of blood products are associated with several complications, many of which can be grouped as immunological or infectious. There is also increasing focus (and controversy) on complications arising directly or indirectly from potential quality degradation during storage.

Immunogic reaction

- *Acute hemolytic reactions* occur with transfusion of red blood cells, and occurs in about 0.016 percent of transfusions, with about 0.003 percent being fatal. This is due to destruction of donor red blood cells by preformed recipient antibodies. Symptoms include fever, chills, chest pain, back pain, hemorrhage, increased heart rate, shortness of breath, and rapid drop in blood pressure. When suspected, transfusion should be stopped immediately, and blood sent for tests to evaluate for presence of hemolysis.
- *Delayed hemolytic reactions* occur more frequently (about 0.025 percent of transfusions) and are due to the same mechanism as in acute hemolytic reactions.

Most blood transfusions go very smoothly. Sometimes mild problems can occur. Very rarely, serious problems occur.
Allergic Reactions - Some people have allergic reactions to the blood given during transfusions. This can happen even when the donated blood is the correct blood type. Allergic reactions can be mild or severe. Symptoms may include: Anxiety Chest or back pain Trouble breathing Fever, A quick pulse or low blood pressure, Nausea (feeling sick to your stomach)

A nurse or doctor will stop the transfusion at the first signs of an allergic reaction. The health care team will figure out the severity of the reaction, what treatments are needed, and whether they can safely restart the transfusion.

4. ORGAN TRANSPLANTATION

Moving an organ from a donor's body to a patient's body, or to create organs from the patient's own stem cells (regenerative medicine as an emerging field) in order to replace the recipient's damaged or absent organ, that is what the term Organ Transplantation refers to, including the following organs.

- Thymus
- Intestine
- Lungs
- Pancreas
- Liver
- Kidneys
- Heart

It also involves to transplantation of tissues such as,

- Bones
- Muscoloskeletal grafts
- Cornea
- Skin
- Heart valves
- Nerves
- Veins

It is one of the most complex and challenging areas of medicine, because of the ever-present risk that the recipient body rejects the transplant, making the removal necessary.

Benefits and Outcomes of Organ Transplant

Organ transplant is the last possibility to address a state of organ failure. Kidney for instance, is the most frequently carried out organ transplant worldwide, and it is considered the best treatment for its cost effectiveness and life quality prospects it restores.

Organ transplantation requires long term health evaluation of the patient. Only academic communities and medical scientists have the right to monitor the outcomes of transplants and regulate donations.

Three Essential Processes

In modern times, doctors and patients face an enormous demand for transplants which has long surpassed the supply of organs. Patients must wait a long time, years in some cases, for a chance to get hold of a donated organ. That's why scientists are working along with politicians to solve this problem.

Organ distribution is therefore the first essential step, followed by the transplant surgery and the follow-up or post-surgery recovery.

Evaluation Process

The following are some components of the transplant evaluation process:

- Psychological evaluation – in which the medical team assesses significant psychological and social issues such as stress, financial situation and family support.
- Blood tests – essential in the selection process to joining the donor's list. They are performed to determine donor match, priority in the list and to improve chances against organ rejection.
- Diagnosis – to assess health status. Includes X-rays, ultrasound, biopsy, dental examinations, among other diagnostic tests depending on the transplant surgery required.

Organ Distribution

When a particular organ fails, transplant can be the only chance for the patient. For procedures like kidney and liver transplant, a willing donor might be found among family members or friends. A very small number of transplants come from people donating as a result of a good, Samaritan gesture. Nevertheless, there is still the necessity of being appropriate for donor-recipient match, a process of selection achieved through serotyping. Then it is possible to proceed with the surgery state.

Patients must find a transplant team or a group of organ surgeons and health professionals, who decide if the patient is a good candidate, based on the attitude, psychological state, medical history and other factors, to be included in the national waiting list for transplantation.

When the organ becomes available, based on the criteria of all relevant information, a recipient, the best match for the organ is chosen. Then the hospital prepares for surgery.

Surgical Procedure

The fully anesthetized patient is injected with anticoagulant to keep the blood from clotting during the transplantation procedure. Doctors connect the hearth-lung machine, in the case of a

heart transplant, or other life-support devices to enable the surgeon to remove the organ without disrupting body functions.

Three types of rejection

Following a transplant surgery, the following three types of rejection might occur:

- Chronic rejection – might last months or years.
- Acute rejection – a few days after transplant and it is the immune response to foreign matter.
- Hyperacute rejection – as soon as the organ is connected to the new body.

Types of Transplant

- Autograft – transplant of tissue from one area of the body to another, using surplus tissue which is regenerative.
- Allograft – transplant of tissue or organ between non-identical members of a species. This transplant might cause rejection due to genetic difference.
- Xenograft or xenotransplant – a transplant from one species to another. Very risky due to rejection.

Individual organs- kidney, liver, heart, lung, bone, skin, hair and pancreas

4.1Kidney transplant:

- Renal transplantation is the preferred treatment for patients with end-stage renal disease. It offers better quality of life and confers greater longevity than long-term dialysis.
- EMPs encounter transplant pts at 2 critical stages:
- Initial doctors to identify potential donors from a pool of critically ill patients who are admitted to hospital.
- They care for pts once they have been transplanted and present with complications related to their immunosuppressive therapy, infections or ARF.
- Diabetic nephropathy accounts for 40% of the diseases resulting in renal transplantation. This subgroup of pts are also more prone to complications after renal transplantation.
- The spectrum of diseases in transplant pts is different from the general population.
- The classical presentation of common medical disorders may be modified by immunosuppressive medication.

The Transplantation Process

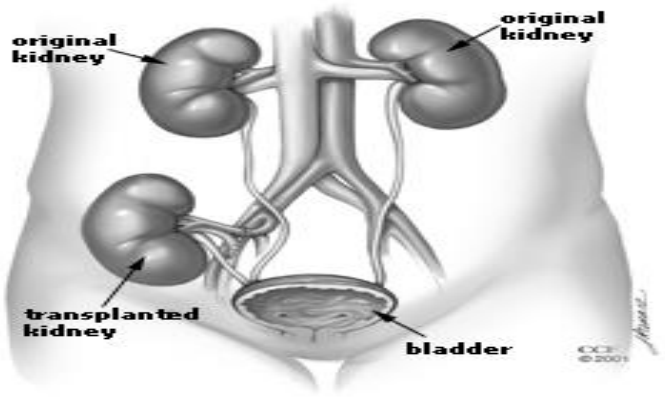
- Transplant coordinators should be called early for any pt who may meet brain death criteria in the new future.

- Absolute C/Is for organ donation include HIV, sepsis, non-CNS malignancy and severe CVS disease.
- Age is also a relative C/I (i.e. organs not harvested from pts >75 years of age).
- The pretransplantation workup of a potential donor includes testing for CMV, HSV, EBV, HIV, Hep A, B, C, D + E and HTLV type 1.

- Following brain death, a number of physiological changes occur that need to be rectified if donor organ perfusion is to be preserved.
- Increased cerebral oedema after trauma or stroke results in catecholamine release and HT.
  With brainstem necrosis, catecholamine levels drop rapidly resulting in hypotension. This should be corrected with fluid and vasopressors
- About 75% of organ donors develop diabetes insipidus due to pituitary necrosis and this leads to hypovolaemia.
- Systemic thermal control is often lost due to hypothalamic ischaemia which results in coagulopathy, hepatic dysfunction and cardiac dysfuction.
- Allograft : graft between genetically dissimilar individuals of the same species.
- Autograft : graft in which donor and recipient are the same individual.
- Xenograft : Donor and recipient belong to different species.

The Surgical Procedure

- Wet ischaemia time (time from cessation of circulation to removal of organ and its placement in cold storage) should not exceed 30 mins.
- Transplanted kidney is placed in the R or L lower quadrant of the abdomen in an extraperitoneal position. On examination, the transplant is easily palpable.
- The transplant renal a is anastomosed to the ipsilateral internal or external iliac a, the renal v to internal or external iliac v and the transplant ureter to the bladder.
- Generally a single kidney is transplanted.
- When small, paediatric or older cadaveric donor kidneys with age-related loss of renal fxn are transplanted, both kidneys from the donor might be placed in a single recipient to provide adequate fxnal renal mass.
- Living donor transplants fxn immediately after transplant, +/- 30% of cadaveric transplants have delayed graft fxn because of more prolonged ischaemic cold preservation. These pts need continued dialysis support until the kidney starts to fxn.



4.2 Liver transplant:

- 1960 :Initial Liver Transplant (LT) techniques done using dogs.
- 1963 : First human LT attempt by Starzl.
- 1967 : First successful LT by Starzl.
- Early 1980's: LT became clinical reality.
- 1983 : Definitive therapy for end-stage liver disease (ESLD).
- 1988: Development of the University of Wisconsin (UW) solution (graft preservation).
- 1992: First Liver xenotransplants x 2 (baboon) by AG Tzakis

Potential Indications for LT

- Viral hepatitis
- Malignant neoplasm of liver and intrahepatic bile ducts
- Benign neoplasm of liver and biliary passages
- Carcinoma of liver and biliary system
- Neoplasm of uncertain behavior in liver and biliary passages
- Neoplasm of unspecified nature in digestive system
- Glycogenesis
- Pure hypercholesterolemia
- Lipidoses
- Disorders of copper metabolism
- Cystic fibrosis, disorders of porphyrin metabolism, other disorders of purine and pyrimidine metabolism, amyloidosis, disorders of bilirubin excretion, mucopolysaccharidosis, other deficiencies of circulating enzymes
- Congenital factor VIII disorder

- Congenital factor IX disorder
- Budd-Chiarri syndrome
- Acute and subacute necrosis of liver
- Alcoholic fatty liver
- Alcoholic cirrhosis of liver
- Chronic hepatitis
- Cirrhosis of the liver without mention of alcohol
- Biliary cirrhosis
- Other chronic nonalcoholic liver disease
- Unspecified liver disease without mention of alcohol
- Other sequelae of chronic liver disease
- Other specified disorders of gallbladder
- Biliary atresia, other anomalies of gallbladder, bile ducts, and liver
- Perinatal jaundice due to hepatocellular damage
- Other specified perinatal disorders of digestive system
- Injury to liver
- Encephalopathy, unspecified
- Portal vein thrombosis

Contraindications to LT

ABSOLUTE	**RELATIVE**
✓ **Active infection** ✓ **SBP** ✓ **Pulmonary HTN** ✓ **Extrahepatic malignancy** ✓ **Active alcoholism** ✓ **Active substance abuse** ✓ **Non compliance**	➢ **CRF** ➢ **Advanced cachexia** ➢ **Large HCCs** ➢ **Multisystem organ failure states** ➢ **HIV**

Liver recipient procedure Orthotropic LT

- Total Hepatectomy (venovenous bypass)
- Caval anastomosis (conventional, Piggyback technique).
- Reperfusion
- Portal vein anastomosis

- Hepatic Artery anastomosis (end to end, infrarenal aortic jump graft)
- Biliary reconstruction (duct – to duct, Roux-en-Y hepatico-jejunostomy).

Living Donor/Split LT

- Living-donor LT: part of the liver from a living donor is resected and transplanted into a recipient.
- Split LT: a whole adult liver is transected into 2 pieces to provide grafts for 2 recipients

Postoperative Care

- Liver function tests monitoring
- Fibrinogen level is the most important indicator of graft function in first 24 hours (> 100).
- Gradual normalization of ALT, AST, T. Bili, PT.
- Early elevation of liver enzymes (LEs) followed by quick normalization is reflective of preservation injury (cold preservation).
- Primary non functional liver: marked increase of (LEs) and T. Bili (Tx: re-transplant).
- Thrombocytopenia: Platelet count decrease in the first week after LT and increase during the second week. (Platelet sequestration in the liver and spleen, preservation injury).
- Doppler US Liver: intra-operatively, and daily until POD# 5. (Velocity and RI of HA, PV, HV flow).
- Daily monitoring of immunosuppressive drug levels.

Immunosuppressant regimens

- ✓ ISP drugs necessary to prevent rejection.
- ✓ The risk of rejection is highest (up to 40%) during the first 3-6 months after transplantation and decreases significantly thereafter.
- ✓ ISP induction: Prograf (FK) + Steroids (OR)
- ✓ Maintenance:
  - Prograf + Steroids
  - Prograf + Campath (steroid free protocol)
  - Rapamycin + Steroids
  - OKT-3 (severe rejection)

4.3Bone Marrow Transplant

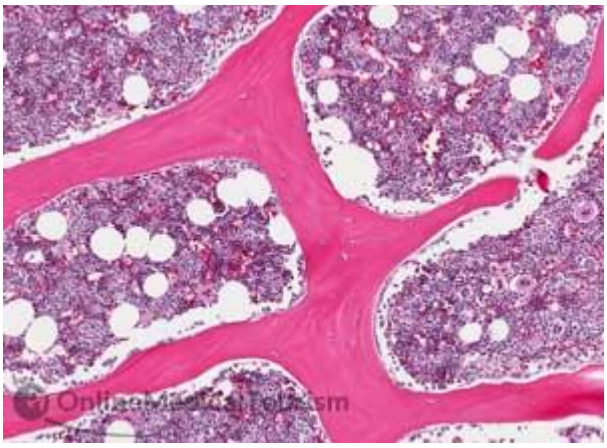
Located in the interior of our bones, bone marrow is one of the areas that we are never concerned with until we have some complaint. However, this flexible, spongy and well-protected tissue is essential for our organism.

A vital component of the bone marrow are stem cells which are immature cells that are able to form a variety of different cells in our body (e.g.: neural cells). Stem cells are responsible for the production of the cellular elements of the blood: red blood cells (carry oxygen), platelets (ensure blood clotting) and lymphocytes (immune functions).

What Are The Most Common Diseases?

- Aplastic anemia (damaged bone marrow and dropped red blood cell production)
- Leukemia (abnormal white cell production)
- Bone marrow cancer

Moreover, cancer radiation and chemotherapy can also severely damage bone marrow. To avoid it, before radiation or chemotherapy treatment of cancer patients their stem cells are harvested from the bone marrow to protect them and after the treatment they are re-injected to restore immune functions.



Diagnosis

Examination of bone marrow tissue can happen by biopsy and bone marrow aspiration to gain information about the source of blood production. The procedure is rather unpleasant but unavoidable.

Bone Marrow Transplant

Bone marrow transplantation can be the only solution to treat some severe diseases, such as:

- bone marrow cancer
- leukemia
- multiple myeloma
- certain blood diseases
- autoimmune diseases

In the procedure stem cells are taken from a healthy donor and infused into the patient to help ideal blood cell production.

Bone Marrow Transplant Procedure

We can distinguish three kinds of bone marrow transplants:

- Autologous (the process of removing and reinjecting the patient's own bone marrow before cancer treatment)
- Umbilical cord blood transplant (stem cells are removed from the baby's umbilical cord for later use)
- Allogenic bone marrow transplant (from donor to patient)

In allogenic procedures, first the matching donor is identified by blood tests (usually family members with similar genes).

Patients' own bone marrow is suppressed by radiation and chemotherapy. It is important in order to remove malfunctioning stem cells and to suppress the immune system that will resist the transplanted cells less.

Stem cells are taken from a donor, who receives general anesthesia while the bone marrow is surgically removed from hip bones.

The stem cells are infused into the bloodstream with a catheter, similarly to a blood transfusion. The stem cells will find their way to the bone marrow.

Bone marrow transplant has many risks and usually involves a lengthy post-treatment.

4.4. Pancreas Transplant

One of the most important functions of the pancreas is to produce insulin, which is a vital hormone that regulates the absorption of glucose (commonly known as blood sugar) into the cells. The main problem with type 1 diabetes is the lack of insulin production in the pancreas, resulting in the increase of blood sugar levels up to dangerous life-threatening conditions.

By far the principal cause for pancreas transplantation is type 1 diabetes. Pancreas transplant defines the surgical procedure in which a healthy donor pancreas is transplanted into a patient

whose pancreas has failed or no longer function properly. Pancreas transplant may have a particularly significant number of side effects and complications and that is why the procedure is only reserved for patients with serious diabetes complications.

Kidney transplant is quite often done in conjunction with pancreas transplants.

Pancreas Transplant – Causes and Risks

Pancreas transplantation is not a standard treatment, because anti-rejection medications, which are usually required for organ donations, in this case can trigger extremely serious complications.

Doctors should make and attempt with all treatments available for pancreatic diseases before recommending pancreas transplantation.

The most common causes for pancreas transplant are:

- Type I diabetes
- Poor blood sugar control
- Insulin reactions
- Severe kidney damage

Pancreas transplant is not a treatment option for Type II diabetes because the problem is not related to insulin production in the pancreas, but in the inability to use insulin properly.

When kidney damage is due to type 1 diabetes, pancreas transplant can be combined with kidney transplantation. These procedures aim to prevent further diabetes-related damage in the future.

Among the risks for pancreas transplant there are some that are commonly related to any type of surgery:

- Infection
- Bleeding
- Blood clots

Severe complications involved in pancreas transplant:

- Hyperglycemia (excess sugar in the blood)
- Urinary complications
- Failure of the donated pancreas
- Rejection of the donated pancreas

Side effects due to anti-rejection medication are frequents such as:

- High cholesterol
- Bone thinning
- High blood pressure
- Skin sensitivity
- Puffiness
- Weight gain
- Acne
- Swollen gums
- Excessive hair growth

Pancreas Transplantation Procedure

The first thing to do is to choose a transplant center, which should be selected from your insurance company's list or from your own selection.

A few things are important to consider:

- Learn about pancreas transplant history of the clinic
- Ask about recipient survival rates
- Compare statistics with the Scientific Registry of Transplant Recipients
- Consider post-op services like support groups, local housing, travel arrangements and referrals

After this, the transplant team will perform an assessment of the patient's eligibility for pancreas transplant. Among the items to consider we find and overall health (can the patient tolerate life-long post-transplant medication?) and life-style habits. Before the procedure, patients have to prepare for numerous lab tests.

When the patient has been accepted, the candidate will be placed on the national waiting list. From this point until the actual pancreas transplantation, waiting time depends on when a suitable donor is available.

During the pancreas transplant, an inpatient surgical procedure done under general anesthesia, an incision is made in the center of the abdomen and the donor pancreas is placed into the lower abdomen. The next step requires the attachments of a piece of donor intestine and of the blood vessels.

The procedure usually lasts three hours or a bit more. After the pancreas transplant, patients stay in the clinic for a few days, till their condition stabilizes and medication routine is established.

4.5 Heart Transplant Surgery

Heart transplant surgery is a major procedure to replace a malfunctioning heart with a healthy donor heart. About 50% of heart transplant patients live 10 years or longer with the new heart, people who otherwise would have little chance of survival on medication or with minor heart surgeries. All potential complications considered, the practice of cardiac transplant is remarkably successful.

Who Is Eligible For Heart Transplant Surgery?

Patients who have tried all other medical and surgical options and are determined to take the necessary lifestyle changes. Eligible patients are usually younger than 65 and have no other life threatening medical problem. The following conditions may call for heart transplantation -

- Inherited and congenital heart defects
- Coronary artery disease
- Cardiomyopathy (weakening heart muscles)
- Diseases of the heart valves

Heart Transplant Procedure

When all other medical means have failed to improve, the physican refers the patient to a heart transplant cencter to evaluate the case and the subject'general health status.

Then the patient is added to the heart transplant waiting list. As there is a global shortage of donor hearts, waiting lists are usually long.

When there is a recently deceased donor, doctors must consider the following aspects before appointing a patient for heart transplant surgery –

- Severity and urgency of the heart failure
- Size of the donor heart
- Blood type

The donor heart must be transplanted within 4 hours of removal so doctors and patients usually do not have much time for contemplation, a decision must be made immediately.

The heart transplant surgery itself is not very long; it takes about 4-5 hours. During the procedure the patient is connected to a heart-lung machine to maintain circulation while the diseased heart is changed to the donor heart. The newly implanted heart receives an electric shock to initiate its beating, but sometimes it starts automatically once the blood flows again in the veins.

For a few days after the operation patients experience heavy breathing, pain and chest pressure, but these side-effects cease after about a week or two. After patients are discharged from hospital, constant check-up is necessary for another three months.

During this period patients will be administered medication to repress your immune system, to reduce the risk that the immune system attacks the foreign tissues. Weakened immune responses should be compensated with antibacterial and antiviral medication.

In the recovery period patients should get used to new lifestyle habits, healthy, regular eating and physical activity. Most cardiac transplant patients can resume their normal activities within 3-6 months but they are instructed to avoid stress and strenuous workout.

The Risks of Heart Transplant Surgery

- Immune rejection of the new heart may occur in the first year post-surgery. In order to monitor it, regular biopsy is taken from the heart. The signs of rejection are very similar to that of the flu: headache, fever, weakness, dizziness and vomiting.
- Artificial weakening of the immune system can be a double-edged sword, which can result in viral and bacterial infections.

In spite of the efficiency of the procedure and the relatively few cases of complication, heart transplant surgery has many downsides that need to be addressed in the future –

- Costs are extremely high, usually several hundreds of dollars
- Insurers' reluctance to cover the costs
- Limited eligibility of patients
- Scarce donor hearts
- Slow channels that do not reach the patient in time.

4.6 Skin Graft

Skin grafting is a type of graft surgery involving the transplantation of **skin**. The transplanted tissue is called a **skin** graft. **Skin grafting** is often used to treat: Extensive wounding or trauma. Burns.

Skin grafting is a surgical procedure that involves removing the skin from one area of the body and moving it, or transplanting it, to a different area of the body. This surgery may be done if a part of your body has lost its protective covering of skin due to burns, injury, or illness.

A skin graft is placed over an area of the body where skin has been lost. Common reasons for a skin graft include:

- skin infections
- deep burns
- large, open wounds
- bed sores or other ulcers on the skin that haven't healed well

There are two basic types of skin grafts: split-level thickness and full-thickness grafts.

Split-Level Thickness Grafts

- A split-level thickness graft involves the removal of the top two layers of skin, the epidermis and the dermis. These layers are taken from the donor site, which is the area where the healthy skin is located.
- Split-level thickness grafts are used to cover large areas. These grafts tend to be fragile and typically have a shiny or smooth appearance. They may also appear paler than the adjoining skin. Split-level grafts don't grow with the rest of the skin, so children who get them may need additional grafts as they grow older.

Full-Thickness Grafts

- A full-thickness graft involves the removal of the muscles and blood vessels in addition to the top two layers of skin from the donor site.
- Full-thickness grafts are generally used for small wounds on highly visible parts of the body, such as the face. Unlike split-level thickness grafts, full-thickness grafts blend in well with the skin around them and usually grow with the person.

Risks for the skin graft surgery are:

- Bleeding
- Infection
- Loss of grafted skin
- Nerve damage
- Graft-versus-host disease

Rejection may occur in xenografts. To prevent this, the patient usually must be treated with long-term immunosuppressant drugs.

4.7 Hair Transplantation

Hair transplantation is a surgical technique that moves hair follicles from a part of the body called the 'donor site' to a bald or balding part of the body known as the 'recipient site'. It is primarily used to treat male pattern baldness. In this minimally invasive procedure, grafts containing hair follicles that are genetically resistant to balding, (like the back of the head) are transplanted to the bald scalp. Hair transplantation can also be used to restore eyelashes, eyebrows, beard hair, chest hair and to fill in scars caused by accidents or surgery such as face-lifts and previous hair transplants. Hair transplantation differs from skin grafting in that grafts

contain almost all of the epidermis and dermis surrounding the hair follicle, and many tiny grafts are transplanted rather than a single strip of skin.

Since hair naturally grows in groupings of 1 to 4 hairs, current techniques harvest and transplant hair "follicular units" in their natural groupings. Thus modern hair transplantation can achieve a natural appearance by mimicking original hair orientation. This hair transplant procedure is called follicular unit transplantation (FUT). Donor hair can be harvested in two different ways: strip harvesting, and follicular unit extraction (FUE).

4.7.1 Pre-operative assessment and planning

At an initial consultation, the surgeon analyzes the patient's scalp, discusses their preferences and expectations, and advises them on the best approach (e.g. single vs. multiple sessions) and what results might reasonably be expected. Pre-operative folliscopy will help to know the actual existing density of hair, so that postoperative results of newly transplanted hair grafts can be accurately assessed.

4.7.2Harvesting methods

Transplant operations are performed on an outpatient basis, with mild sedation (optional) and injected local anesthesia. The scalp is shampooed and then treated with an antibacterial agent prior to the donor scalp being harvested.

There are several different techniques for harvesting hair follicles, each with their own advantages and disadvantages. Regardless of the harvesting technique, proper extraction of the hair follicle is paramount to ensure the viability of the transplanted hair and avoid transection, the cutting of the hair shaft from the hair follicle. Hair follicles grow at a slight angle to the skin's surface, so transplanted tissue must be removed at a corresponding angle.

There are two main ways in which donor grafts are extracted today: strip excision harvesting, and follicular unit extraction.

4.7.2.1Strip harvesting

Strip harvesting is the most common technique for removing hair and follicles from a donor site. The surgeon harvests a strip of skin from the posterior scalp, in an area of good hair growth. A single-, double-, or triple-bladed scalpel is used to remove strips of hair-bearing tissue from the donor site. Each incision is planned so that intact hair follicles are removed. The excised strip is about 1–1.5 x 15–30 cm in size. While closing the resulting wound, assistants begin to dissect individual follicular unit grafts, which are small, naturally formed groupings of hair follicles, from the strip. Working with binocular Stereo-microscopes, they carefully remove excess fibrous and fatty tissue while trying to avoid damage to the follicular cells that will be used for grafting.

The surgeon then uses very small micro blades or fine needles to puncture the sites for receiving the grafts, placing them in a predetermined density and pattern, and angling the wounds in a consistent fashion to promote a realistic hair pattern. The technicians generally do the final part of the procedure, inserting the individual grafts in place.

Strip harvesting will leave a thin linear scar in the donor area, which is typically covered by a patient's hair even at relatively short lengths. The recovery period is around 2 weeks and will require the stitches/staples to be removed by medical personnel or sub cuticular suturing can be done.

4.7.2.2 Follicular unit extraction (FUE)

With Follicular Unit Extraction or FUE harvesting, individual follicular units containing 1 to 4 hairs are removed under local anesthesia; this micro removal typically uses tiny punches of between 0.6mm and 1.0mm in diameter. The surgeon then uses very small micro blades or fine needles to puncture the sites for receiving the grafts, placing them in a predetermined density and pattern, and angling the wounds in a consistent fashion to promote a realistic hair pattern. The technicians generally do the final part of the procedure, inserting the individual grafts in place.

FUE takes place in a single long session or multiple small sessions. The FUE procedure is more time consuming than strip surgery. An FUE surgery time varies according to the surgeons experience, speed in harvesting and patient characteristics. The procedure can take anywhere from a couple hours to extract 200 grafts for a scar correction to a surgery over two consecutive days for a megasession of 2,500 to 3,000 grafts. With the FUE Hair Transplant procedure there are restrictions on patient candidacy. Clients are selected for FUE based on a fox test, though there is some debate about the usefulness of this in screening clients for FUE.

FUE can give very natural results. The advantage over strip harvesting is that FUE harvesting negates the need for large areas of scalp tissue to be harvested, so there is no linear incision on the back of the head and it doesn't leave a linear scar. Because individual follicles are removed, only small, punctuate scars remain which are virtually not visible and any post-surgical pain and discomfort is minimized. As no suture removal is required, recovery from Micro Grafting FUE is less than 7 days.

Disadvantages include increased surgical times and higher cost to the patient. It is challenging for new surgeons because the procedure is physically demanding and the learning curve to acquire the skills necessary is lengthy and tough. Some surgeons note that FUE can lead to a lower ratio of successfully transplanted follicles as compared to strip harvesting.

Follicular unit transplant

Follicular unit transplant (FUT) is the traditional hair transplant method which involves extracting a linear strip of hair bearing skin from the back or the side of the scalp. The strip is then dissected to separate individual grafts.

Robotic hair restoration

Robotic hair restoration devices utilize cameras and robotic arms to assist the surgeon with the FUE procedure.

5. Regeneration and humans

Regeneration in humans is the regrowth of lost tissues or organs in response to injury. This is in contrast to wound healing, which involves closing up the injury site with a scar. Some tissues such as skin and large organs including the liver regrow quite readily, while others have been thought to have little or no capacity for regeneration. However ongoing research, particularly in the heart and lungs, suggests that there is hope for a variety of tissues and organs to eventually become regeneration-capable.

Regeneration means the regrowth of a damaged or missing organ part from the remaining tissue. As adults, humans can regenerate some organs, such as the liver. If part of the liver is lost by disease or injury, the liver grows back to its original size, though not its original shape. And our skin is constantly being renewed and repaired. Unfortunately many other human tissues don't regenerate, and a goal in regenerative medicine is to find ways to kick-start tissue regeneration in the body, or to engineer replacement tissues.

Understanding how regeneration works

Recent research in different regenerating animals has shown that there are various stem cell strategies for regenerating body parts built from multiple tissues, such as muscle, nerve and skin.

Naturally regenerating appendages and organs

Endometrium

The endometrium after the process of breakdown via the menstruation cycle, re-epithelializes swiftly and regenerates. Though tissues with a non-interrupted morphology, like non-injured soft tissue, completely regenerate consistently; the endometrium is the only human tissue that completely regenerates consistently after a disruption and interruption of the morphology.

Fingers

In May 1932, L.H. McKim published a report in *The Canadian Medical Association Journal*, that described the regeneration of an adult digit-tip following amputation. A house surgeon in the Montreal General Hospital underwent amputation of the distal phalanx to stop the spread of an infection. In less than one month following surgery, x-ray analysis showed the regrowth of bone while macroscopic observation showed the regrowth of nail and skin. This is one of the earliest recorded examples of adult human digit-tip regeneration.

Studies in the 1970s showed that children up to the age of 10 or so who lose fingertips in accidents can regrow the tip of the digit within a month provided their wounds are not sealed up with flaps of skin – the de facto treatment in such emergencies. They normally won't have a fingerprint, and if there is any piece of the finger nail left it will grow back as well, usually in a square shape rather than round.

In August 2005, Lee Spievack, then in his early sixties, accidentally sliced off the tip of his right middle finger just above the first phalanx. His brother, Dr. Alan Spievack, was researching regeneration and provided him with powdered extracellular matrix, developed by Dr. Stephen Badylak of the McGowan Institute of Regenerative Medicine. Mr. Spievack covered the wound with the powder, and the tip of his finger re-grew in four weeks. The news was released in 2007. Ben Goldacre has described this as "the missing finger that never was", claiming that fingertips regrow and quoted Simon Kay, professor of hand surgery at the University of Leeds, who from the picture provided by Goldacre described the case as seemingly "an ordinary fingertip injury with quite unremarkable healing"

A similar story was reported by CNN. A woman named Deepa Kulkarni lost the tip of her little finger and was initially told by doctors that nothing could be done. Her personal research and consultation with several specialists including Badylak eventually resulted in her undergoing regenerative therapy and regaining her fingertip.

Kidney

Regenerative capacity of the kidney has been recently explored.

The basic functional and structural unit of the kidney is nephron, which is mainly composed of four components: the glomerulus, tubules, the collecting duct and peritubular capillaries. The regenerative capacity of the mammalian kidney is limited compared to that of lower vertebrates.

In the mammalian kidney, the regeneration of the tubular component following an acute injury is well known. Recently regeneration of the glomerulus has also been documented. Following an acute injury, the proximal tubule is damaged more, and the injured epithelial cells slough off the basement membrane of the nephron. The surviving epithelial cells, however, undergo migration, dedifferentiation, proliferation, and redifferentiation to replenish the epithelial lining of the proximal tubule after injury. Recently, the presence and participation of kidney stem cells in the tubular regeneration has been shown. However, the concept of kidney stem cells is currently

emerging. In addition to the surviving tubular epithelial cells and kidney stem cells, the bone marrow stem cells have also been shown to participate in regeneration of the proximal tubule, however, the mechanisms remain controversial. Recently, studies examining the capacity of bone marrow stem cells to differentiate into renal cells are emerging.

Like other organs, the kidney is also known to regenerate completely in lower vertebrates such as fish. Some of the known fish that show remarkable capacity of kidney regeneration are goldfish, skates, rays, and sharks. In these fish, the entire nephron regenerates following injury or partial removal of the kidney.

Liver

The human liver is particularly known for its ability to regenerate, and is capable of doing so from only one quarter of its tissue, due chiefly to the unipotency of hepatocytes. Resection of liver can induce the proliferation of the remaining hepatocytes until the lost mass is restored, where the intensity of the liver's response is directly proportional to the mass resected. For almost 80 years surgical resection of the liver in rodents has been a very useful model to the study of cell proliferation.

Toes

Toes damaged by gangrene and burns in older people can also regrow with the nail and toe print returning after medical treatment for gangrene

Future research and regenerative medicine

By defining the properties of stem cells that regenerate complex body parts, scientists are learning how injury causes these stem cells to regenerate the missing part instead of just forming scar tissue.

Ethical considerations of Tissue engineering

Different approaches address ethical considerations of tissue engineering: research ethics, socioeconomic issues and anthropological issues.

Research ethics

- When asking the consent of cell donors, it is important to inform them of the use of their tissue. But will researchers explain clearly what they will do with the cells and what kind of tests they will perform? Will the information provided be sufficient?
- Can the human body and its parts be subject to property rights?

Socioeconomic issues

- What will be the cost of tissue engineering products and treatments?
- Who will finance the research? The government or the private sector?
- Who will be given priority to receive these treatments? Young people with congenital diseases or the elderly who suffer from degenerative diseases?

Anthropological issues

- Is it ethically right to fight the negative effects of ageing? Is extending life always a good thing?
- Have we thought about the consequences of having an ageing society?