LECTURES 16-17: ARTIFICIAL HEART AND LUNG ASSIST DEVICES

16.1 Transplantation types

16.1.1 Autograft

Autografts are the transplants 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).

16.1.2 Allograft 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.

16.1.3 Isograft

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.

16.1.4 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 an 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, xenotransplantation 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 histocompatibility 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.

16.2 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 cardio vascularly stable, parenteral iron is a preferred option based on both efficacy and safety

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16.3 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
• Musculoskeletal 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.

16.3.1 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.

16.3.2 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.

16.3.3 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.

16.4 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.

16.5 Types of Transplants

- 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

16.6 Kidney 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.

16.6.1 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.

16.7 Bone 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).

16.7.1 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.

16.7.2 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.

16.7.3 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.

16.7.4 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.

16.8 Liver Transplant

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.

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.

16.9 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.

16.9.1 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

16.9.2 Severe complications involved in pancreas transplant:

• Hyperglycemia (excess sugar in the blood)

• Urinary complications

• Failure of the donated pancreas

• Rejection of the donated pancreas

16.9.3 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

16.9.4 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.

16.9.5 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.

16.10 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

16.10.1Heart 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.

16.10.2 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.

16.11 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.

16.11.1 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.

16.12 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).

16.13 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"

16.14 Ethical considerations of Tissue engineering

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

16.14.1 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?