

# Transplantation

Ist Department of Surgery, St. Anne's University Hospital Brno

# Transplantation

- ▶ A medical procedure in which an organ, part of an organ or tissue is transferred from one place to another or from one body to another
- ▶ To replace a damaged or missing organ
- ▶ The aim to restore functions
- ▶ Graft - tissue that is transplanted without reconstruction of the vascular bed (skin, muscle,...)
- ▶ Transplant - organ transplantation with concomitant reconstruction of vascular bed
- ▶ In practice, both terms are used as synonyms

# History

- ▶ 1902 Ulmann - kidney transplantation in a dog
- ▶ 1912 Carrel and Guthrie - have developed a transplantation technique based on a perfect vascular stitch
- ▶ 1933 Voronoj - kidney transplantation from deceased to young woman with renal failure due to mercury poisoning (graft did not restore function, recipient died)
- ▶ 1943 Medawar - knowledge of the immunological cause of rejection
- ▶ 1958 Dausset - discovery of histocompatible antigens (HLA)
- ▶ Introduction of immunosuppressive therapy (whole body irradiation, later medication)
- ▶ 1963 Starzl - has contributed to the development of liver transplants
- ▶ 1963 Hardy - first lung transplantation
- ▶ 1966 Kelly and Lillehei - pancreatic transplantation
- ▶ 1967 Barnard - first successful heart transplant using Shumway technique

# Types of transplantation by tissue origin

- ▶ Autograft (autotransplantation)
  - ▶ Transplant of tissue to the same person
  - ▶ There is no risk of graft rejection
    - ▶ Skin, blood vessels
- ▶ Allograft (allotransplantation)
  - ▶ Between two genetically non-identical members of the same species
  - ▶ There is a risk of graft rejection, immunosuppressants are needed
    - ▶ Donor
    - ▶ Recipient
- ▶ Xenograft (xenotransplantation)
  - ▶ From one species to another (e.g. porcine heart valve transplant)
- ▶ Isograft (syngeneic)
  - ▶ From a donor to a genetically identical recipient (such as an identical twin)
  - ▶ Do not trigger an immune response
- ▶ Implantation
  - ▶ Transplantation of artificial, synthetic tissue

# Types of transplants by location

- ▶ Orthotopic transplantation
  - ▶ The previous organ is removed and the transplant is placed at that location in the body (e.g. heart into the mediastinum)
- ▶ Heterotopic transplantation
  - ▶ The transplant is placed in a different location in the host than it had been in the donor - e.g. kidney transplant is placed in the anterior part of the lower abdomen, in the pelvis

# Immunological aspects

- ▶ MHC (Major Histocompatibility Complex) - the genetic system responsible for recognizing one's own from the alien
- ▶ In humans, the major histocompatibility system is the HLA complex (Human Leucocyte Antigen) - complex of genes that determine surface antigens
- ▶ 5 HLA complexes - HLA-A, HLA-B, HLA-C, HLA-D, HLA-DR
- ▶ Consensus in tissue HLA antigens between donor and recipient facilitates graft acceptance and prevents or attenuates post-transplant immune response
- ▶ Graft from HLA identical sibling recipient tolerates
- ▶ Graft from HLA unrelated individual is not tolerated
- ▶ The greater HLA conformity, the longer graft survival
- ▶ Identification of HLA antigens - tissue typing
  - ▶ Serological and cellular methods replace DNA typing.
- ▶ HvG - host versus graft - recipient's immune response against histocompatible antigens of graft

# Immunological aspects

- ▶ GvH - graft versus host - transplantation of immunocompetent cells, graft's T-lymphocytes response against recipient antigens
  - ▶ Hematopoietic stem cells
  - ▶ Small intestine, lungs, sometimes liver (contain a lot of lymphatic tissue)
- ▶ Rejection does not occur:
  - ▶ Autotransplantation
  - ▶ Syngeneic transplantation
  - ▶ Tissue transplants that do not express histocompatible antigens (bones, tendons, cartilage)
  - ▶ Transplantation to immunologically privileged place - lymphocytes can't get there (e.g. brain, eye, gonades)
- ▶ Immunosuppressants
  - ▶ Chemotherapeutics - corticosteroids, cyclosporin A, FK506 (Tacrolimus), Rapamycin, Sanghlifehrin A, Azathioprine, Mycophenolate, mofetil, Cyclophosphamide, Deoxyspergualin, Chlorambucil, Methotrexate, Brequinar, Leflunomid, FTY720, Tautomycetin,
  - ▶ Monoclonal, polyclonal antibodies - antilymphocytic globulin, antithymocyte globulin, OKT3, CAMPATH, anti-CD25, anti-CD4, anti-CD8, anti-CD2, anti-LFA3
  - ▶ Total body irradiation

# Transplant rejection

## ▶ Hyperacute

- ▶ The existence of preformed antibodies against donor antigens
- ▶ Graft destruction within minutes to hours
- ▶ Vascular thrombosis and necrosis
- ▶ The crossmatch is a protection

## ▶ Accelerated

- ▶ Lower antibody titer, within 5 days after transplantation

## ▶ Acute

- ▶ Most common, within three months and later
- ▶ Activation of T-lymphocytes against graft antigens with interstitial inflammation
- ▶ Graft function is decreased
- ▶ Increase of immunosuppressive therapy

## ▶ Chronic

- ▶ Gradual deterioration of graft function due to vascular changes
- ▶ Predominantly humoral factors
- ▶ Months to years



# Rejection

- ▶ Deterioration of laboratory parameters (e.g. increases of urea, creatinine)
- ▶ Decrease in graft function (e.g. diuresis)
- ▶ Verification by needle biopsy
- ▶ Decrease in graft function can be caused e.g. by nephrotoxicity of cyclosporine

# Transplantation centers in the Czech Republic

- ▶ IKEM Prague
  - ▶ Kidneys, heart, pancreas, liver, small intestine, uterus
- ▶ UH Motol Prague
  - ▶ Lungs, kidneys
- ▶ CKTCH Brno
  - ▶ Heart, liver, kidneys
- ▶ UH Olomouc
  - ▶ Kidneys
- ▶ UH Ostrava
  - ▶ Kidneys
- ▶ UH Hradec Králové
  - ▶ Kidneys
- ▶ UH Pilsen
  - ▶ Kidneys

# Conditions for transplantation

## 1. surgical technique

- ▶ Revascularization by vascular anastomoses
- ▶ Connection of organ ducts (ureter, bile duct, pancreatic duct), intestinal anastomoses or respiratory tract
- ▶ Grafting without damage
- ▶ Preservation of graft function by intensive care
- ▶ Complications:
  - ▶ Fistula of ducts
  - ▶ Graft thrombosis (mostly leads to graft loss)
  - ▶ Oppression of ureter caused by accumulation of lymph around the transplanted kidney

# Conditions for transplantation

## 2. source of organs

- ▶ Living donors
  - ▶ Paired organ (kidneys) or part of organ (liver)
  - ▶ Close relative (parents, children, siblings)
  - ▶ Emotionally related (husband and wife)
  - ▶ Unrelated donor
- ▶ Deceased donors
  - ▶ Sudden death, esp. craniotrauma, spont. bleeding, ischemia after resuscitation, after drowning, in some cases meningitis or a primary brain tumor

- ▶ Warm ischemia
  - ▶ Time from organ procurement to start of perfusion with perfusion solution
  - ▶ Start: MAP < 50 mmHg or SpO<sub>2</sub> 70%
  - ▶ End: start flushing
  - ▶ Rapid cell damage
  - ▶ Most organs tolerate only a few minutes, it should not exceed 30 minutes
  - ▶ Nearly zero warm ischemia can be achieved in donors with a beating heart
- ▶ Cold ischemia
  - ▶ Start: start flushing
  - ▶ End: restoration of blood flow
  - ▶ It should not exceed 36 to 48 hours
  - ▶ Tolerance time (kidneys up to 36 hours), (heart, liver, pancreas, lungs 6-12 hours)
- ▶ Graft half-life: was defined as the time taken for 1/2 of the grafts functioning at 1 year to fail
- ▶ Organ Transplant Act

# Clinical determination of brain death

- ▶ Brain death
  - ▶ is the complete loss of brain function (including involuntary activity necessary to sustain life). It differs from persistent vegetative state, ordinary coma, condition known as locked-in syndrome
- ▶ Exclusion of factors affecting consciousness
  - ▶ E.g. hypothermia, hypoxia, intoxication, effect of drugs, hypoglycemia
- ▶ Neurological examination
- ▶ The assessment is carried out by two physicians with specialized competence

# Clinical determination of brain death

- ▶ Examination of brainstem reflexes
  - ▶ Pupillary light reflex
  - ▶ Corneal reflex
  - ▶ Oculocephalic reflex
  - ▶ Gugging reflex
  - ▶ Cough reflex
  - ▶ Oculovestibular reflex
  - ▶ Apnea test

# Apnea test

- ▶ To confirm breathing center malfunction
- ▶ Disconnecting the patient from ALV
- ▶ CO<sub>2</sub> is accumulated, which physiologically stimulates the respiratory center
- ▶ If damaged, the patient is unable to ventilate spontaneously
- ▶ In COPD patients, it may not be valid, elevated CO<sub>2</sub> may not be a sufficient incentive to activate the center



# Clinical determination of brain death

## ▶ Paraclinic examinations

- ▶ CT angiography - partially preserved circulation may occur in decompressive craniotomies, ventricular drainage and small children
- ▶ Evoked potential test
- ▶ Transcranial Doppler ultrasound
- ▶ Digital subtraction angiography
- ▶ Cerebral perfusion scintigraphy
- ▶ Electroencephalography

# Another donor examination

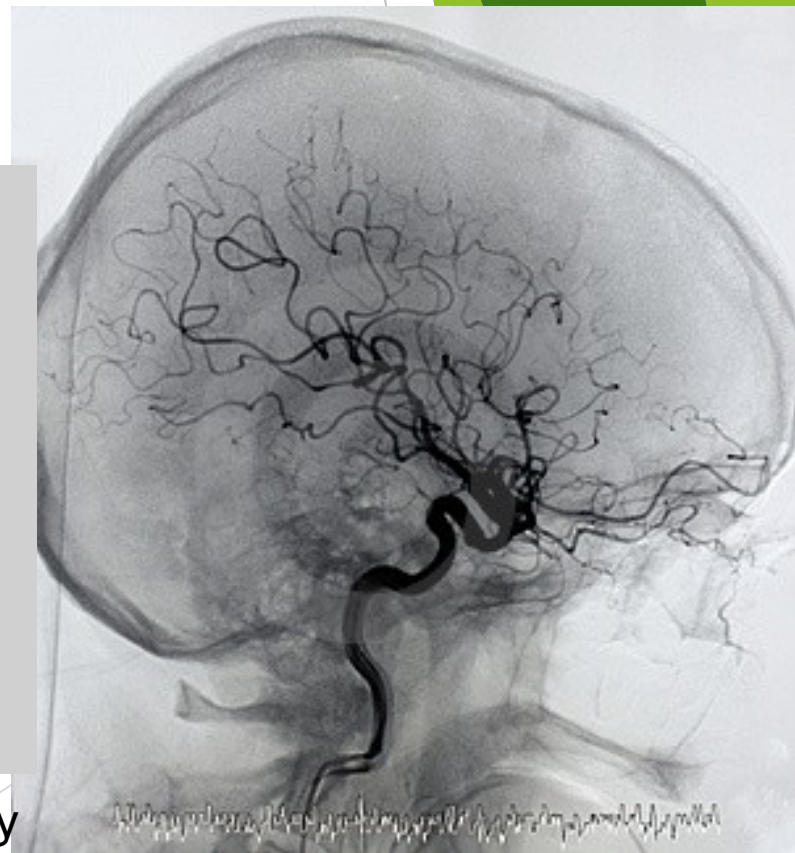
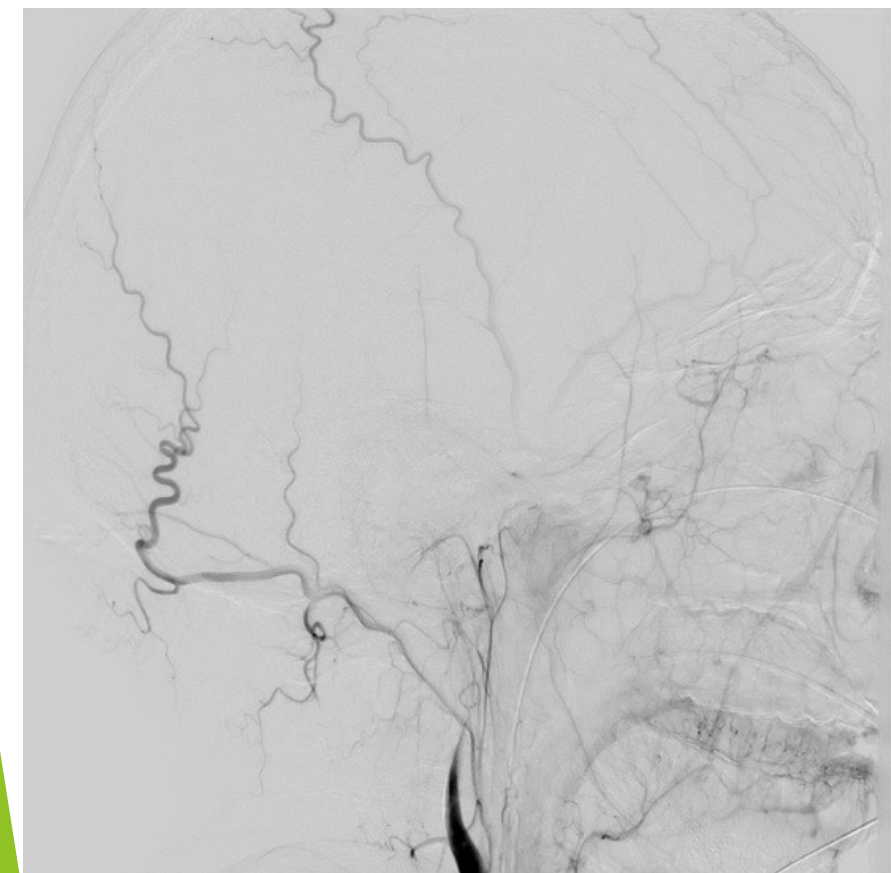
- ▶ Virology + Serology: TPHA, HBsAg, anti - HBC total, antibodies against HIV 1 a 2, anti CMV (IgM a IgA), EBV.
- ▶ Biochemical profile: Na, K, Cl, Gly, urea, creatinine, osmolality, AST, ALT, ALP, GGT, Bilirubin, Albumin, CB, AMS, CK, CKMB, Trop-T, Myoglobin, CRP.
- ▶ Blood count, coagulation, blood type, Rh factor
- ▶ Astrup
- ▶ Electrocardiography
- ▶ ECHO
- ▶ Coronarography
- ▶ X-ray
- ▶ Abdominal ultrasound
- ▶ Examinations are indicated in cooperation with the transplant coordinator

# Absolute contraindications to transplantation

- ▶ Bacterial sepsis (except milder forms)
- ▶ AIDS
- ▶ Tuberculosis
- ▶ HBV
- ▶ HCV
- ▶ Malignancy (except isolated brain, skin, in situ cervix carcinoma)
- ▶ Long-term hemodialysis
- ▶ Patient disagreement with transplantation
- ▶ Impossibility to identify the patient
- ▶ Noncompliance of recipient

# Donor care

- ▶ Rule 100
- ▶ Blood pressure 100/80 mmHg
- ▶ Diuresis 100ml/h (according to the patient's weight)
- ▶ Normothermia
- ▶ Hb >100g/l
- ▶ Normoglycemia
- ▶ Saturation 99%
- ▶ Fluid resuscitation
- ▶ Maintaining ions and acid-base balance
- ▶ Venous access: CVC, NG tube, PUC, arterial catheter
- ▶ To inform survivors



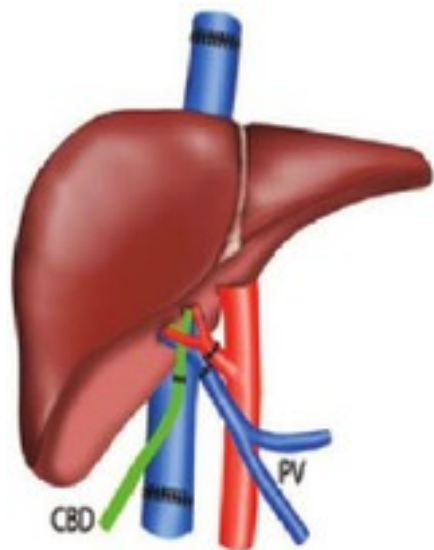
Physiological angiography

# Liver transplantation

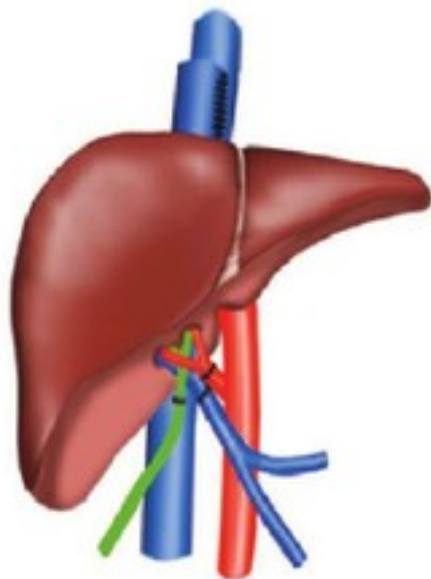
- ▶ The first successful liver transplantation in 1967 (USA)
- ▶ The first liver transplantation in the Czech republic in 1983 in St. Anne's University Hospital Brno led by prof. Kořístka
- ▶ In the Czech Republic two centers - IKEM Prague and CKTCH Brno
- ▶ Most common indications: biliary cirrhosis, alcoholic, chronic active hepatitis, sclerosing cholangitis, congenital atresia of the biliary tract, Wilson's disease, alpha-1-antitrypsin deficiency, Budd-Chiari syndrome and hemochromatosis
- ▶ Controversial in primary malignancies due to frequent relapses
- ▶ Orthotopically
- ▶ Often only one lobe or segment in children
- ▶ Technically demanding - liver artery, portal vein, inferior vena cava, bile ducts
- ▶ Economic demands - the need for a number of blood derivative transfers - portal hypertension, coagulation disorders
- ▶ Need 10-15 per million inhabitants per year
- ▶ 85 candidates were on the waiting list in 3.5.2019
- ▶ 58 liver transplants were performed in CKTCH, 158 in IKEM in 2018



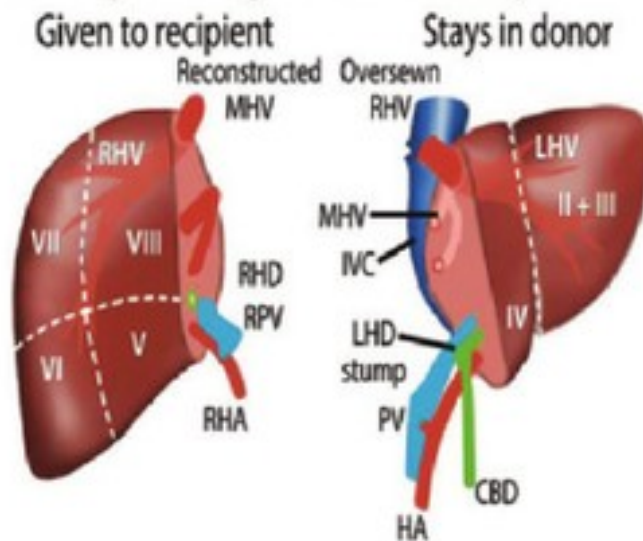
### A. Conventional technique



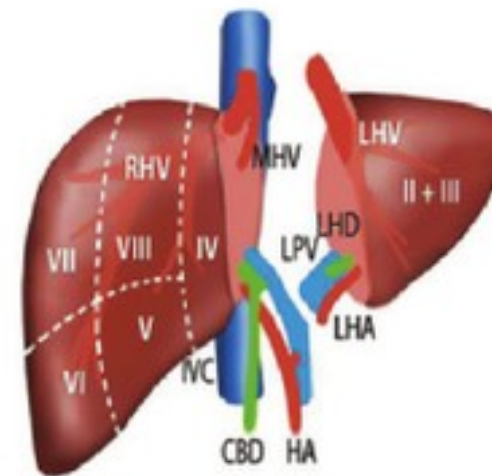
### B. Piggyback technique



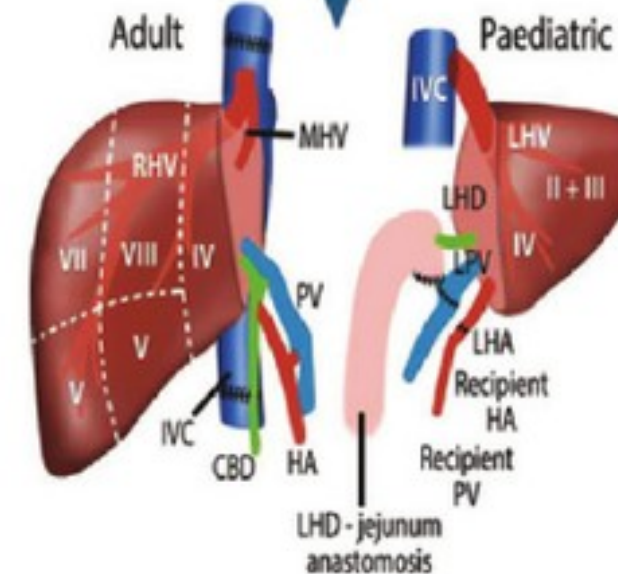
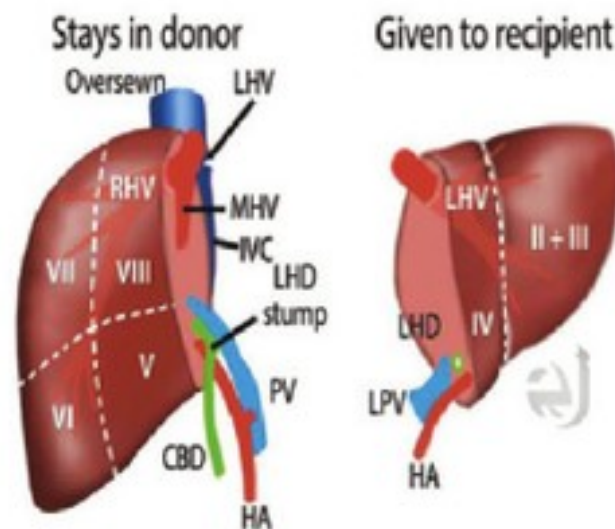
### C. Living donor right lobe liver transplantation



### D. Split liver



### E. Living donor left lobe liver transplantation

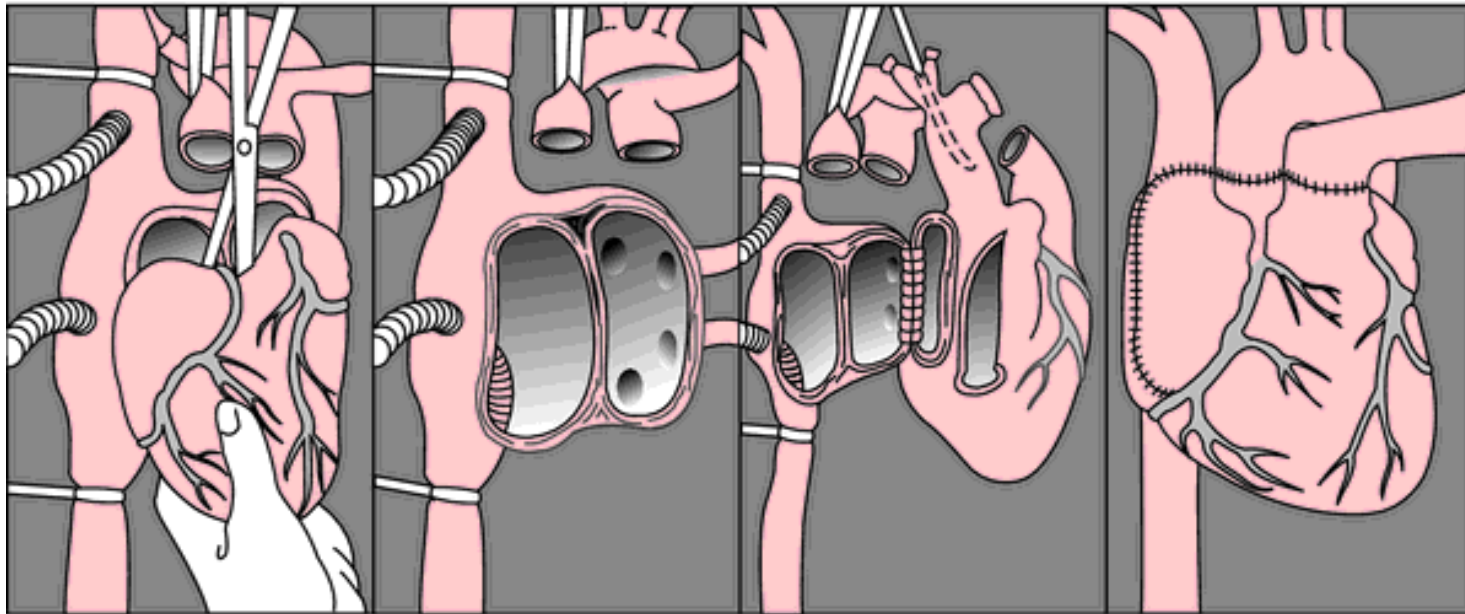


- IVC Inferior vena cava
- HA Hepatic artery
- PV Portal vein
- CBD Common bile duct
- LHA Left hepatic artery
- LPV Left portal vein
- LHD Left hepatic duct
- LHV Left hepatic vein
- RHA Right hepatic artery
- RPV Right portal vein
- RHD Right hepatic duct
- RHV Right hepatic vein
- MHV Middle hepatic vein

# Heart transplantation

- ▶ The first successful heart transplantation was performed by Christiaan Neethling Barnard in 1967
- ▶ In the Czech Republic two centers - IKEM Prague and CKTCH Brno
- ▶ Most commonly indicated in idiopathic dilated cardiomyopathy or ischemic disease (with a prognosis of survival less than 1 year), unmanageable arrhythmias
- ▶ Usually orthotopically (heterotopically supports the heart function of the recipient)
- ▶ Remaining posterior atrial wall with orifices of venae cavae and pulmonary veins, left atrial anastomosis, septum, right atrium, aorta and pulmonary artery
- ▶ Need about 15 per million inhabitants
- ▶ 76 candidates were on the waiting list in 3.5.2019
- ▶ Number of transplants in 2018: 39 IKEM, 35 CKTCH





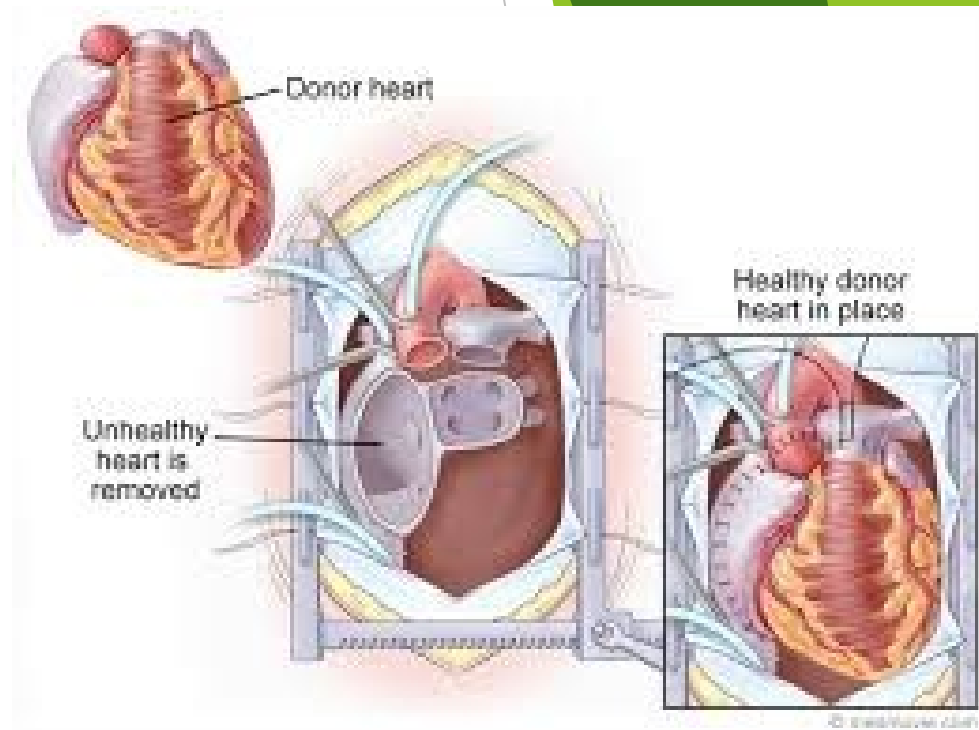
1. After the recipient is placed on cardiopulmonary bypass, the heart is removed.

2. The posterior walls of the recipient's left and right atria are left intact.

3. The left atrium of donor heart is anastomosed to the recipient's residual posterior atrial walls, and the other atrial walls, the atrial septum, and the great vessels are joined.

POSTOPERATIVE RESULT

<https://medical-dictionary.thefreedictionary.com/orthotopic+transplantation>



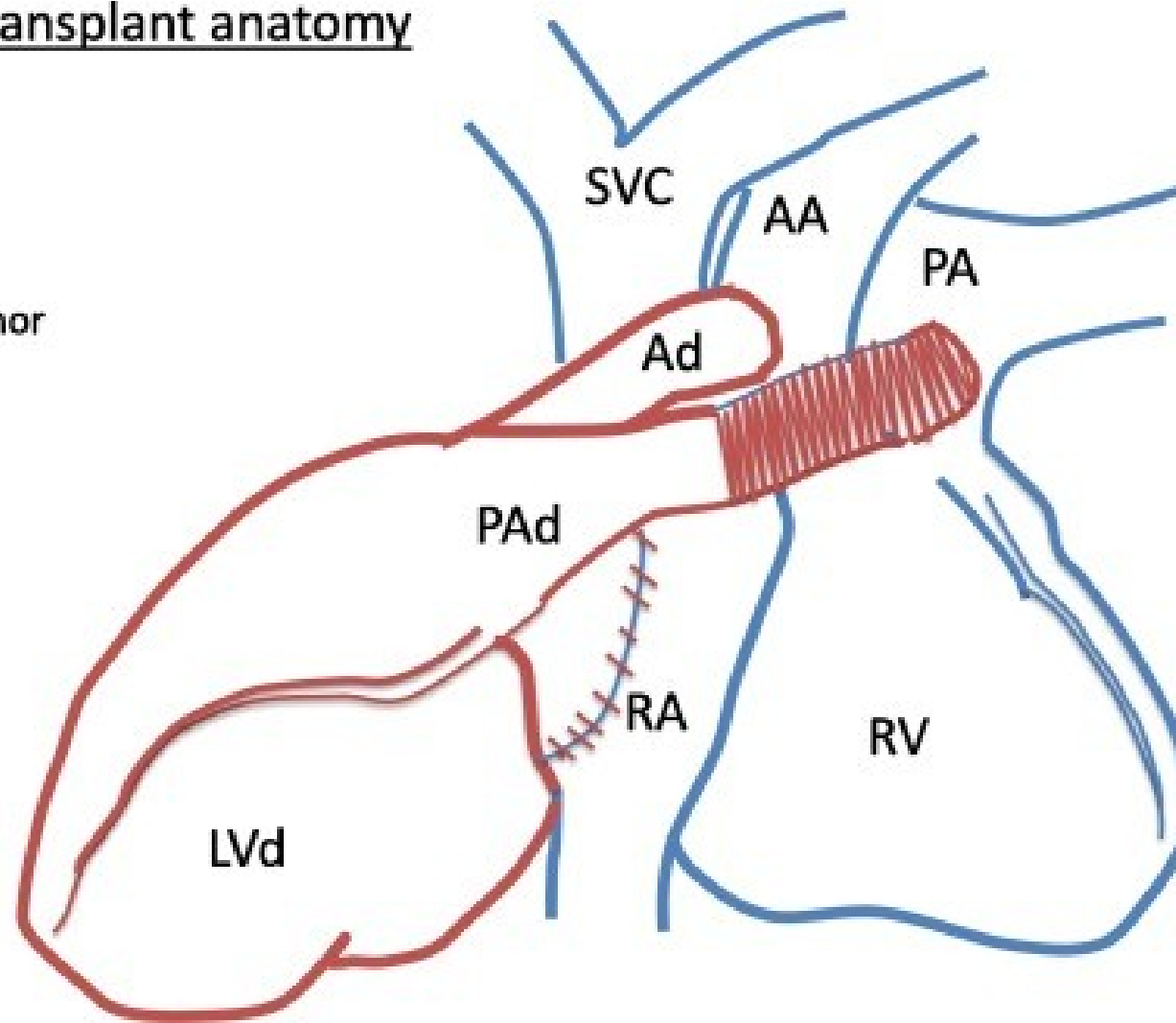
[https://medmovie.com/library\\_id/3255/topic/ahaw\\_0093a/](https://medmovie.com/library_id/3255/topic/ahaw_0093a/)

## Heterotopic heart transplant anatomy

### KEY

LVd Left ventricle, donor  
PAd Pulmonary artery, donor  
Ad Aortic root, donor

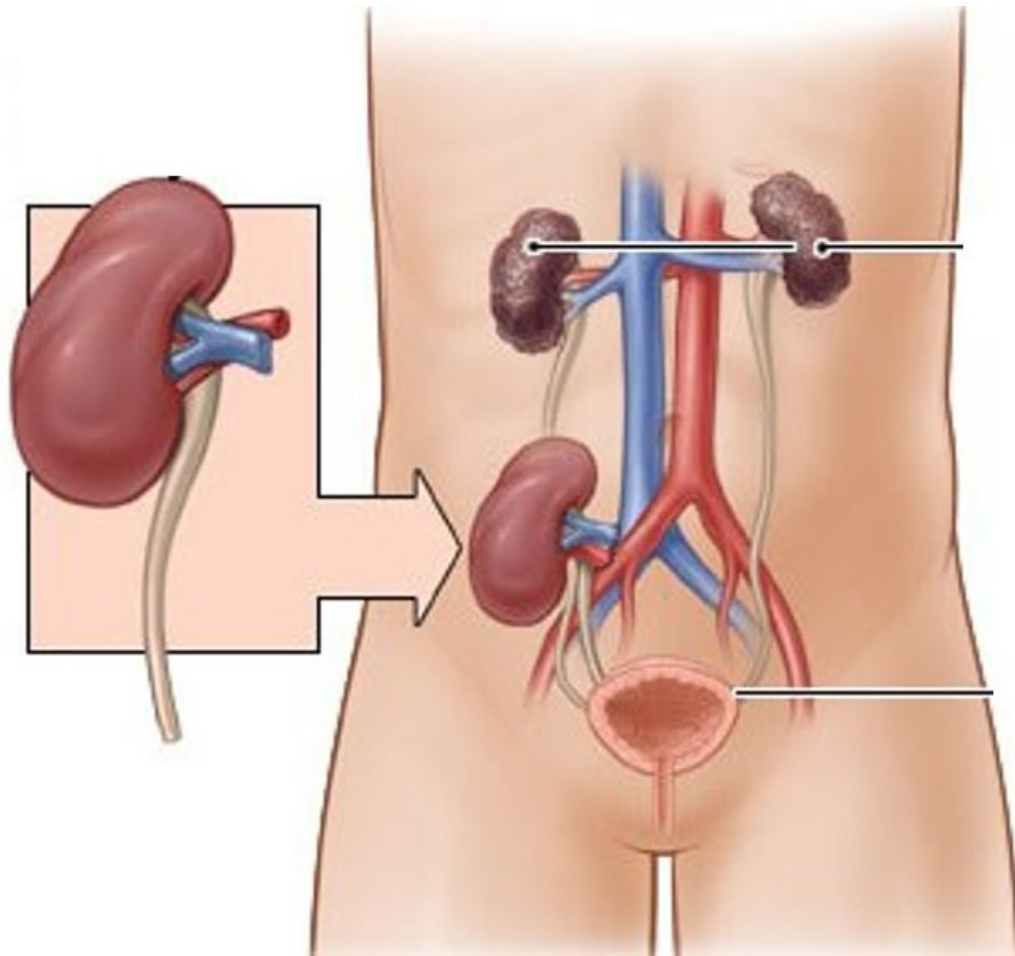
SVC Superior vena cava  
RV Right ventricle  
AA Aortic arch  
PA Pulmonary artery  
RV Right ventricle



# Kidney transplantation

- ▶ First kidney transplant between identical twins in Paris and Boston in 1958
- ▶ Fastest development due to the possibility of hemodialysis during graft failure
- ▶ Indication - 4th stage of chronic renal insufficiency
  - ▶ Glomerulopathy, chronic tubular disease, diabetic nephropathy, polycystosis
- ▶ Heterotopic transplantation to the iliac fossa - blood vessels on the iliac artery and vein, ureter on the bladder
- ▶ Mostly one kidney, rarely transplant of both
- ▶ The original kidney is left unless it is a source of infection, hypertension or polycystosis
- ▶ Living donor transplants have significantly better results, ideally before hemodialysis
- ▶ The kidney usually works immediately after transplantation, sometimes later (days, weeks), in 1/10 never

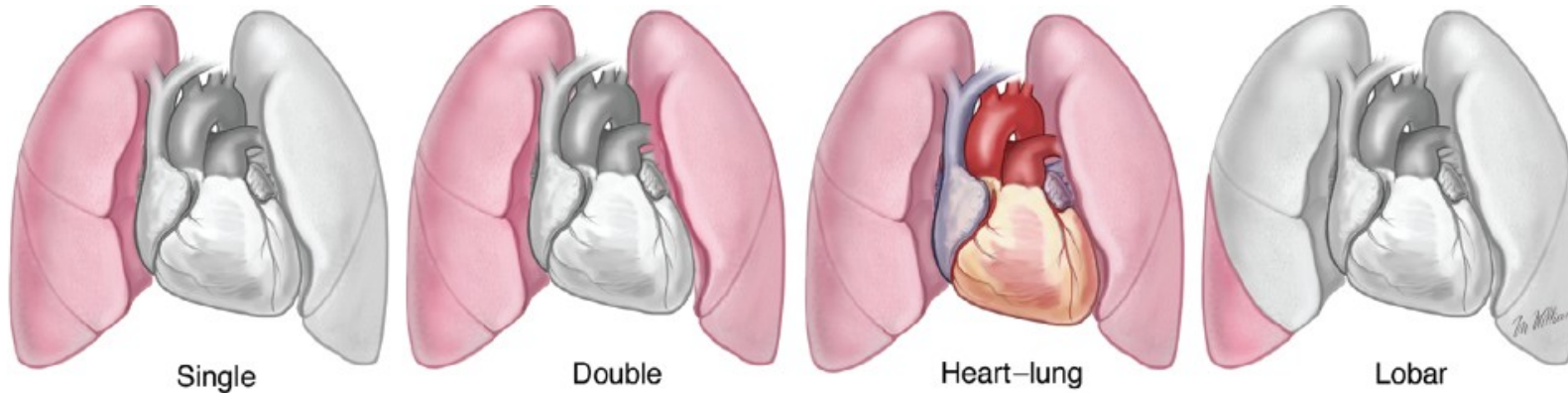
# Kidney transplantation



# Lung transplantation

- ▶ In the Czech Republic since 1997, FN Motol
- ▶ Before transplantation mostly dependence on oxygen therapy
- ▶ Indications: idiopathic pulmonary fibrosis, exogenous allergic alveolitis, histiocytosis X, sarcoidosis, pulmonary emphysema, COPD, cystic fibrosis, pulmonary hypertension
- ▶ One side, both sides, complexed with the heart, lobar is not performed in the Czech Republic
- ▶ Use of extracorporeal circulation
- ▶ Complications: pulmonary edema, pneumonia, arrhythmia, rejection
- ▶ In the Czech Republic 30-50 per year

# Lung transplantation



Source: D. J. Sugarbaker, R. Bueno, Y. L. Colson, M. T. Jaklitsch, M. J. Krasna, S. J. Mentzer, M. Williams, A. Adams: *Adult Chest Surgery*, 2nd ed. Philadelphia, PA: Elsevier; 2007. Copyright © McGraw-Hill Education. All rights reserved.

<https://accesssurgery.mhmedical.com/content.aspx?sectionid=72434315&bookid=131>

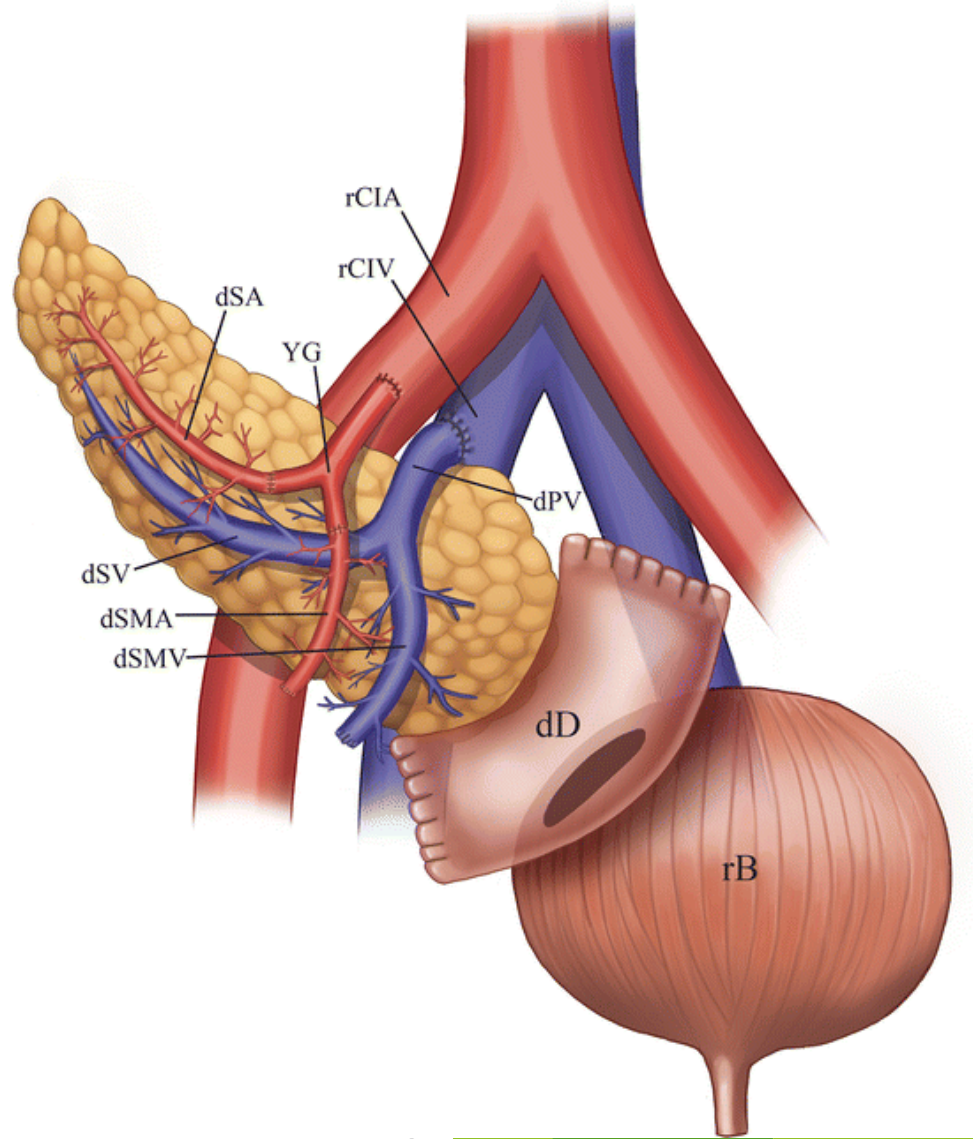
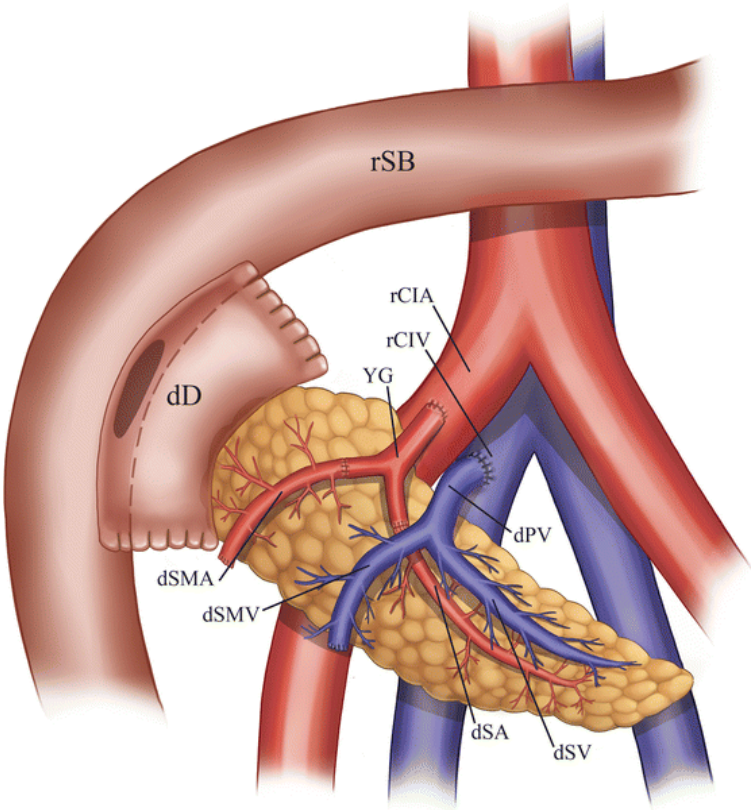
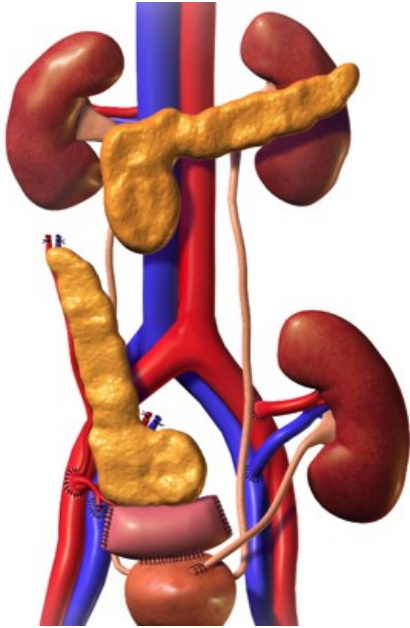
<https://www.mayoclinic.org/tests-procedures/lung-transplant/about/pac-20384754>

# Pancreas transplant

- ▶ IKEM in the Czech Republic
- ▶ Mostly in patients who have had or are waiting for a kidney transplant. Isolated pancreatic transplantation when the risks of poorly controllable diabetes outweigh the risks of long-term immunosuppression.
- ▶ A successful pancreas transplant will eliminate the need for insulin injections, reduce or eliminate dietary and activity restrictions due to diabetes, and decrease or eliminate the risk of severe low blood sugar reactions
- ▶ Artery is anastomosed to right external iliac artery
- ▶ Terminal diabetic nephropathy, type I diabetes mellitus, seldom type II
- ▶ Extraperitoneal, intraperitoneal
- ▶ The need to resolve exocrine secretion - most often the graft duodenum is connected to the jejunal loop, the connection to the bladder is associated with greater complications, polymer obliteration of the outlet, ligation
- ▶ Complications: metabolic, urological, hematological, gastrointestinal, surgical



# Pancreas transplant





# Pancreatic islet cell transplant

- ▶ IEQ/kg - islet equivalent- one IEQ is considered equivalent to a pancreatic islet with a diameter of 150  $\mu\text{m}$
- ▶ The Edmonton protocol - involves isolating islets from a cadaveric donor pancreas using a mixture of enzymes called Liberase
- ▶ Each recipient receives islets from one to as many as three donors
- ▶ Islet cells taken from a deceased donor's pancreas are injected into a portal vein that takes blood to the liver
- ▶ More than one injection of transplanted islet cells may be needed
- ▶ Patients with diabetic nephropathy and obese are contraindicated

# Dermal transplantation

- ▶ Auto-, allo-, xenotransplantation
- ▶ By thickness
  - ▶ Split - thickness - including the epidermis and part of the dermis.
    - ▶ It can be processed through a skin mesher which makes apertures onto the graft, allowing it to expand up to nine times its size.
    - ▶ The donor site heals by re-epithelialisation from the dermis and surrounding skin and requires dressings.
  - ▶ Full - thickness - consists of the epidermis and the entire thickness of the dermis.
    - ▶ The donor site is either sutured closed directly or covered by a split-thickness skin graft.
  - ▶ Composite graft - is a small graft containing skin and underlying cartilage or other tissue
- ▶ Scalpel, Wattson knife, airdermatom, electrodermatome
- ▶ Meshing
- ▶ Extensive wounding or trauma, burns, areas of extensive skin loss due to infection, specific surgeries that may require skin grafts for healing to occur

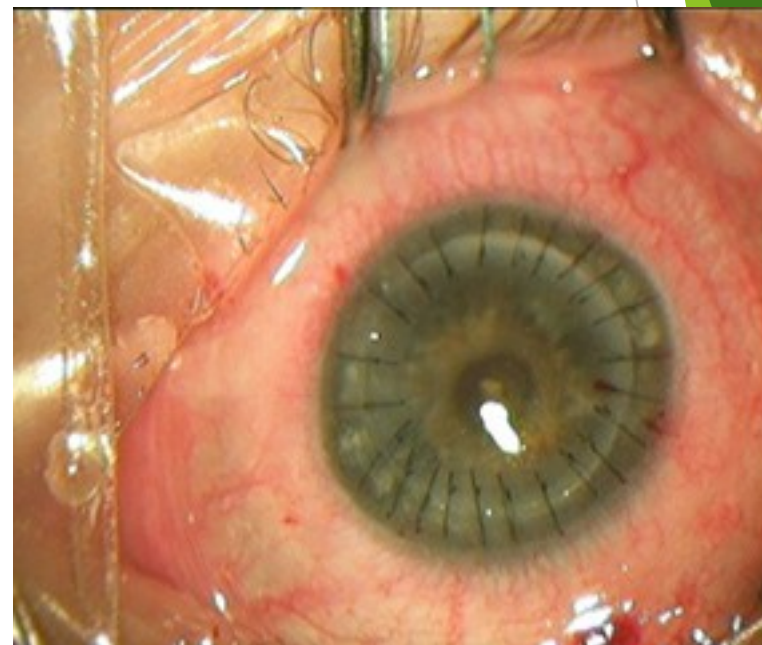
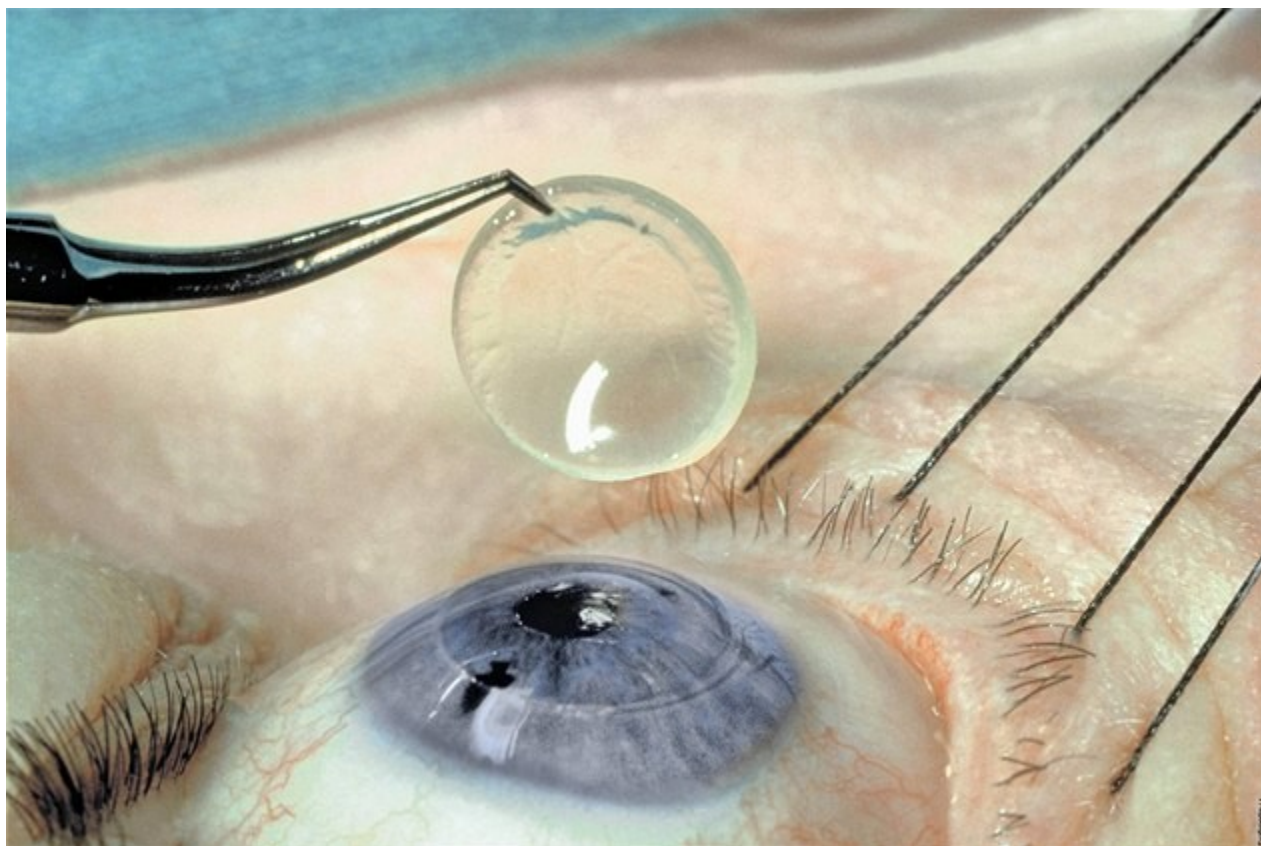
# Dermal transplantation



# Corneal transplantation

- ▶ First in 1905 in Olomouc
- ▶ Perforating keratoplasty - corneal transplantation in full thickness
- ▶ Lamellar keratoplasty - removal of only the damaged or diseased epithelium and stroma, leaving the endothelium intact, in cases where only the more superficial layers are damaged
- ▶ Indications
  - ▶ Optical - transparency restore
  - ▶ Tectonic - preservation of the integrity of the bulb when the cornea is thinning with imminent perforation
  - ▶ Therapeutic - severe inflammations
  - ▶ Cosmetic - blind eyes with leukoma
- ▶ Immunosuppressive treatment is usually discontinued after removal of stitches between 11-13. month
- ▶ Donor-recipient compatibility is not required

# Corneal transplantation



# Stem cell transplant

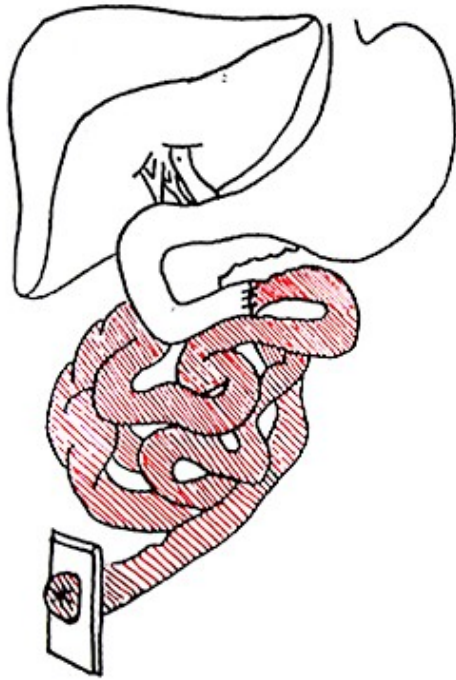
- ▶ Collecting stem cells:
  - ▶ Stem cells from the bone marrow - most often taken from the pelvic bones
  - ▶ Stem cells from the peripheral blood - growth factors, such as G-CSF or plerixafor, may be given for a few days to stimulate stem cells to grow faster and move into the blood from the bone marrow. Machine separates and collects stem cells from the blood.
  - ▶ Stem cells from the umbilical cord
- ▶ Stem cells are given through a central venous catheter and they settle in the bone marrow and begin to multiply and mature
- ▶ Autologous, Allogeneic, Syngeneic
- ▶ Indications: acute myeloid leukemia, acute lymphocytic leukemia, non-Hodgkin's lymphoma, malignant lymphogranuloma, myelodysplastic syndrome, myelofibrosis, chronic lymphocytic leukemia, chronic myeloid leukemia, severe aplastic anemia, myeloma, congenital haematopoietic disorders
- ▶ Graft vs. host disease
- ▶ More than 350 centers in Europe are performing over 18,000 transplantations a year



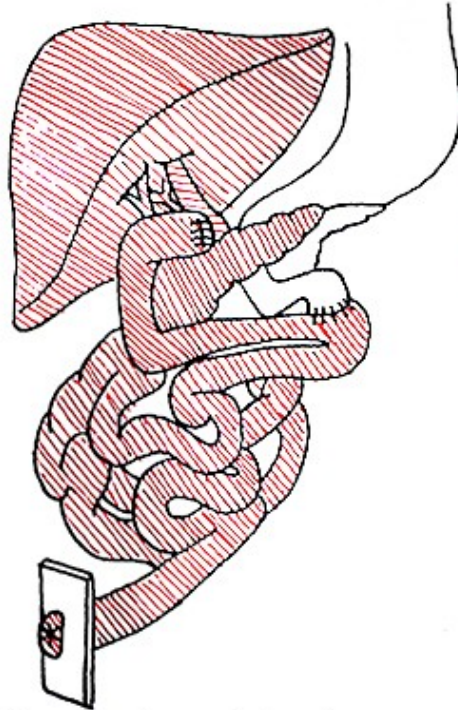
# Small intestine transplantation

- ▶ Four indications:
  - ▶ a loss of two of the six major routes of venous access
  - ▶ multiple episodes of catheter-associated life-threatening sepsis
  - ▶ fluid and electrolyte abnormalities in the face of maximal medical therapy
  - ▶ parenteral nutrition associated liver disease
- ▶ Intestinal failure is usually the result of one of the following:
  - ▶ short bowel syndrome
  - ▶ chronic intestinal pseudo-obstruction
  - ▶ intra-abdominal non-metastasizing tumors
- ▶ The most common causes for intestinal failure in the adult: ischemia, Crohn's disease, trauma, motility disorder, tumor, volvulus
- ▶ The most common causes for intestinal failure in the pediatric: necrotizing enterocolitis, gastroschisis, omphalocele, intestinal atresia, volvulus, intestinal pseudo-obstruction, microvillus inclusion disease, intractable diarrhea of infancy, autoimmune enteritis, intestinal polyposis, Hirschprung disease
- ▶ Complete parenteral nutrition - complications limit permanent use - hepatic impairment, steatosis, fibrosis, cirrhosis, liver failure, catheter sepsis
- ▶ Multivisceral transplantation: intestine, liver, stomach, duodenum, pancreas

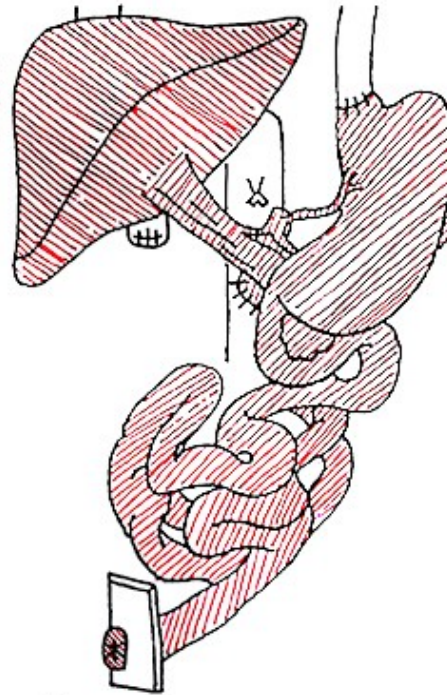
# Small intestine transplantation



A) Isolated small bowel transplantation



B) Liver and small bowel transplantation



C) Multivisceral transplantation



# Others

- ▶ Uterus
- ▶ Face
- ▶ Bones and tendons
- ▶ Heart valves
- ▶ Blood vessels
- ▶ Penis
- ▶ Hand