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ORGAN HARVESTING AND PRESERVATION

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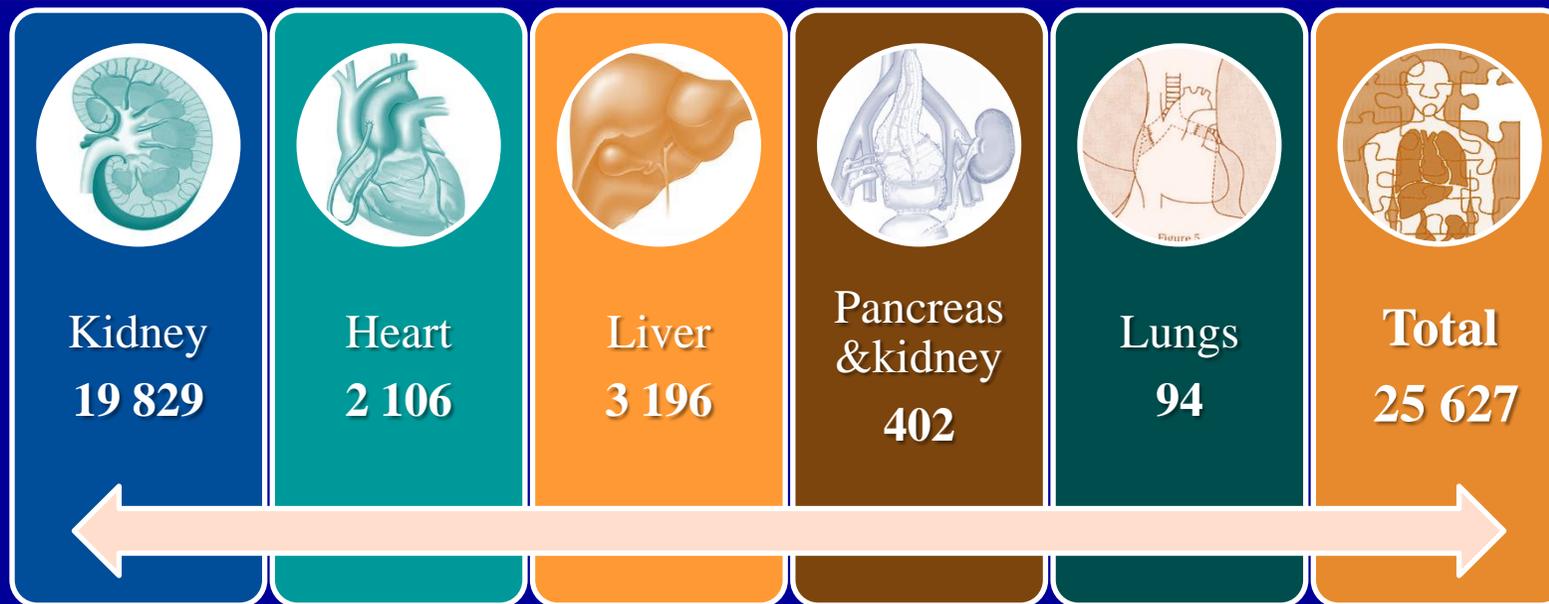


**Department of General Surgery
and Transplantology**

Fact

17 people a day die waiting for a second chance at life.

The number of organ transplants in Poland 1966-2013r



The longest survival of transplant recipients in Poland.

Kidney	from 1976
Heart	from 1987
Liver	from 1995
Pancreas & kidney	from 1991



Types of transplants

- Heterotopic or Orthotopic



- Autograft: same being
- Isograft/Syngenic graft: identical twins
- Allograft/homograft: same species
- Xenograft/heterograft: between species

Organ harvesting and preservation goals

- Good quality organs for transplantation
- Protect organs from ischemic injury
- Preserve all anatomical structures
(vessels, urinary system, bile tract, duodenum)

Transplantation of cells, tissues and organs in Poland

Hematopoietic cells:

Bone marrow
Umbilical cord
blood
Stem cells of
peripheral blood

Tissues:

„biostatic
transplants”
Heart valves
Eye tissues

Vascularized organs:

Kidney
Liver
Pancreas
Heart
Lung
Limb



Methods of Donation

- **Living donation**
 - directed donation
 - non-directed (“Good Samaritan”- USA)
 - exchange donation
- **Deceased donation**
 - Brain death
 - Cardiac death (non-heart-beating donors)

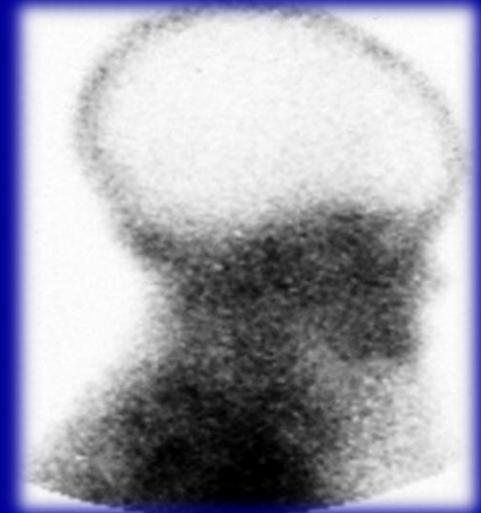
Living Donor Process

- Initial screening (compatibility)
- Medical evaluation
- Psychosocial evaluation
- Informed consent
- Transplant
- Post-transplant care and follow-up

Deceased Donation Process

Brain Death

- “irreversible cessation” of the entire brain including the brain stem
- deep coma, no response to pain, no reflexes, APNEA
- Testing done by physicians who are NOT members of transplant team
- **Brain Death is Death**



Donors for tissue and organ transplantation

1. **Deceased donors (> 96% transplanted organs and tissues)**
 - **allogeneic (allografts) grafts**
 - a. **brain-dead donors whose heart is still beating**
 - all organs and tissues
 - b. **non-heart-beating donors - Immediate rescue of organs after cardiac death (OP on site – most often ER)**
 - **kidneys (some attempts with liver and pancreas), tissues**
2. **Emotionally or genetically-related donors (< 4%)**
 - **allo- or izogeneic grafts**
 - **single kidney, segments of liver, part of pancreas, lobe of lung**
3. **Xenogeneic donors – experimental**

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DECEASED DONORS

2 kidneys

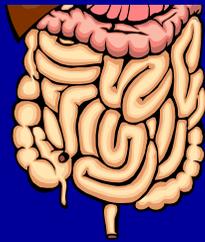
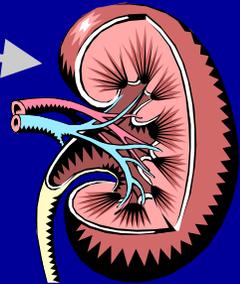
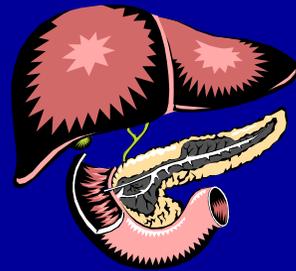
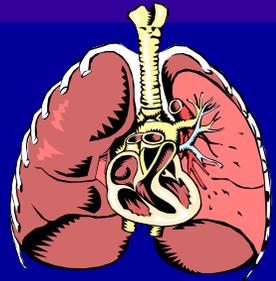
heart

pancreas

liver

2 lungs

small bowel



Tissues: corneas, fascias, valves, bones, vessels

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Cadaveric donors

causes of death

Cerebral vascular accidents	~ 55%
CNS trauma	~ 36%
Other (e.g. CNS ischemia due to heart arrest, asphyxia)	~ 9%
CNS primary tumors	~ historical

Multiorgan harvesting

Goal: to obtain and transplant a number of organs from the same donor

All brain-dead patients are potentially multiorgan donors

single organ harvesting the most often involves only kidneys and tissues

Goals of Donor Care

- Maintain cardiac output
- Maintain fluid and electrolyte balance
- Ensure adequate ventilation and pulmonary stability
- Maintain tissue perfusion
- Prevent infection
- Control diabetes insipidus
- Regulate body temperature

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The donor's actual physiologic status

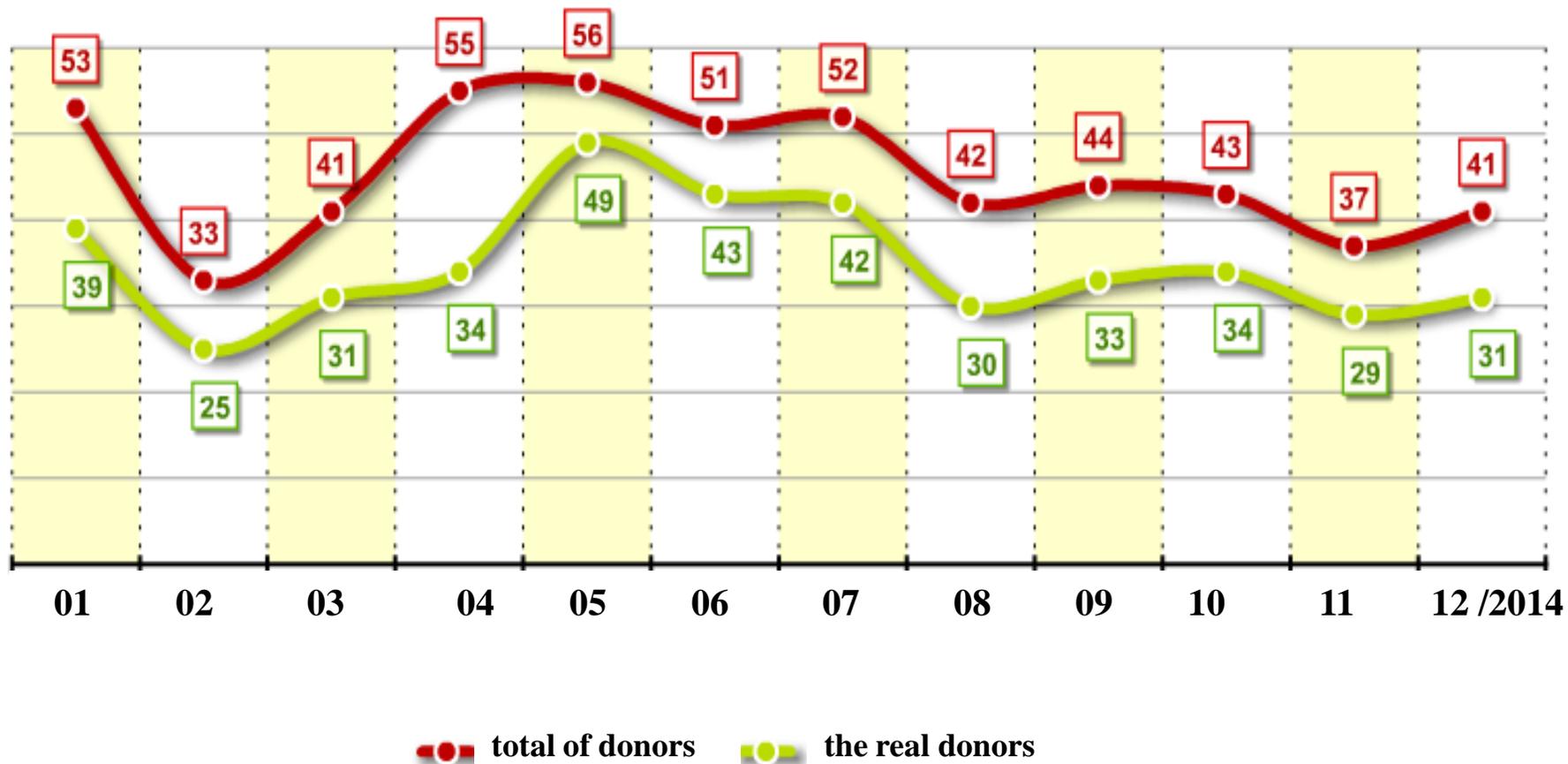
is assessed on

- **arterial blood pressure** (an arterial line is placed if not already present),
- **central venous pressure (CVP),**
- **urine output,**
- **arterial blood gases values,**
- **blood chemistry.**
- **blood type**

Donor categories

- A – hemodynamically stable; systolic pressure (SP) > 100 mmHg, spontaneous diuresis > 100 mL/h; PaO₂ > 100 mmHg; CVP ~ 10 cm H₂O, only with colloids and crystalloids iv for pressure maintenance**
- B - hemodynamically unstable, on dopamine < 10µg/kg/min iv for SP maintenance > 100 mmHg.**
- C - hemodynamically unstable with oliguria / anuria, poor responder to iv fluids, on high dose of dopamine or on some pressors for SP maintenance > 60 mmHg.**

Deceased donors



Contraindications

Relative:

- Physiological age older than 65 years
- Mild hypertension
- DM
- Treated infections
- Intestinal perforation with spillage
- Alcoholism
- Malignancy other than skin that is in remission (>5 y)

Contraindications

Absolute:

- Positive serologic findings of HIV infection
- Systemic sepsis
- Disseminated intravascular coagulation
- Active malignant disease
- Intravenous drug abuse
- Long warm ischemia = long CPR

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„ Malignant neoplasm at present time or in the past”

- **Current or past history of cancer is a contraindication to donation**
- **Exceptions:** basal cell carcinoma of the skin
cervical cancer "in situ"
some of brain tumors not giving metastases

According to Penn et al., may be considered organ transplantation from a donor with a 10 year remission of tumor

There is no universal agreement

Organ donation is excluded from patients with a history of:

- breast cancer
- lung cancer
- melanoma
- sarcoma

„ Malignant neoplasm at present time or in the past”

It is recommended to use following actions :

- ✓ history and physical examination
- ✓ laboratory tests
- ✓ radiological studies
- ✓ examination of organs during harvesting
- ✓ histopathological examination in some cases
- ✓ post-mortem examination

Other tumor markers than

beta-HCG and PSA

are not recommended

due to the low specificity and rarity of occurrence

(requires EBM)

HIV, HCV and HBV tests

mandatory:

- anti HIV
- HBSAg
- anti-HCV
- anti-HBc

Assessment of tests to detect HIV infection

- serological tests ELISA III generation - the reduction of serological window to 25 days
- determination of viral p24 antigen - a reduction of serological window to 14 days
- determination of the viral genome (RNA or PCR-DNA) - reduction of serological window to **11 days**

Standardy wykorzystania narządów do przeszczepienia od zmarłych dawców zakażonych wirusami HIV, HCV, HBV oraz częstość stwierdzenia markera w populacji zmarłych dawców w Polsce.

Status wirusologiczny dawcy	Przeszczepienie		
	nerek	wątroby	serca
anty-HIV dodatni (0,3%)	bezwzględne przeciwwskazanie		
HBsAg dodatni (0,9%)	bezwzględne przeciwwskazanie		
anty-HBc dodatni (16%)	tak (odpowiednio dobranym biorcom)	tak (odpowiednio dobranym biorcom)	tak (odpowiednio dobranym biorcom)
anty-HCV dodatni (2,6%)	tak (odpowiednio dobranym biorcom)	nie przeszczepia się	nie przeszczepia się

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„Risky“ behavior = risk of disease transmission

- drug addiction
- prostitution
- multiplicity of sexual partners
- tattoo made in casual place in the last 12 months
- being in malarial areas, regions of HTLV infection wide (Africa, Japan, Caribbean)

NOTE

Negative virological tests in this group of potential donors - **means nothing**

Prostitution and drug abuse are absolute contraindications to harvesting and transplant organs

Other diseases at present or in the past that can be transferred

Generalized infection - acute infection

Acceptable harvesting – conditions

- hemodynamically stable donor - no symptoms of septic shock
- known source of infection - not derived from an organ which is to be the subject of harvesting
- the infection is not caused by multi-resistant strains
- targeted therapy not less than 48 hours
- prophylactic treatment of a recipient not less than 10 days

CONTROLLED

Harvesting contraindicated - conditions:

- the infection is the cause of death
- septic shock with multiple organ dysfunction
- fungal septicemia
- fungal colonization in the lung
- active tuberculosis
- meningitis caused by *L. monocytogenes*, *M. tuberculosis*, fungi and protozoa
- infection with multi-resistant strain
- do not harvest organ which are source of infection

UNCONTROLLED

Age of the donor and organ function

ECD - American criteria for marginal kidney donor (UNOS '2002)

Fundamental criterion – age

- Age > 60 years
- Age > 50 years and 2 to 3 additional risk factors:
 - hypertension
 - cerebrovascular disease (but not cephalo-cerebral trauma)
as a cause of death
- creatinine > 1.5 mg / dl

Very young donor:

- functional immaturity of organs
- more susceptible to rejection processes
- high risks resulting from technical difficulties

Biologically „age-related injury”

- kidneys - glomerulosclerosis
- heart - atherosclerosis
- pancreas – reduction of amount of islets
over 30 years of age

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The principle of kidney allocation

donor < 16 yo  **pediatric recipient**

donor > 65 yo  **recipient > 50 yo**

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Cadaveric donors

„Ideal" donor

- **20-30 years old**
- **healthy**
- **good tissue perfusion and oxygenation**
- **short time on ICU**
- **good function of organs planned to be transplanted**

Heart donor

- Age < 55
- No h/o heart diseases
- No chest trauma
- No wall motion abnormalities
- short time on ICU
- Normal CXR
- Normal isoenzymes and ECG
- Dopamin infusion < 10 $\mu\text{g}/\text{kg}/\text{min}$
- No CPR

Liver donor

- 55 > Age > 5
- ICU < 7 days
- Systolic pressure > 80 mmHg
- Hypotension (systolic pressure < 80 mmHg)
< 20 min during hospitalization
- CVP > 5 cm H₂O
- PaO₂ > 100 mmHg
- No CPR
- Dopamine infusion < 10 µg/kg/min
- AST, ALT < 100 IU/L
- bilirubin < 2 mg/dL
- No clotting abnormalities

Pancreas donor

- $40 > \text{Age} > 5$
- Amylase level not exceeding 3 x NL
- No h/o DM
- No h/o hypotension longer than 20 min
- No h/o pancreatitis
- No h/o alcohol abuse

Kidney donor

- Age : 5 - 70 years old
- urea < 100 mg/dL
- creatinine < 3.5 mg/dL
- diuresis > 0.5 mL/kg/hour

Organ Preservation

Method used to keep organs viable between procurement and transplantation.

Preservation offers four major advantages to a transplant program

- Time to transport the organ
- Time to allow tissue matching
- Time to prepare the recipient and surgical team
- Quality of organ function; better post-op recovery

Organ Preservation

The time in which organs and tissues can be kept outside the body depends on:

- the organ,
- the type of preservation fluid,
- the preservation method (pump or cold storage).

Organ Preservation Solutions

Optimal preservation solution has to:

- **Ensure rapid hypothermia of organs**
- **Prevent cellular swelling**
- **Avoid biochemical injury**

Organ Preservation Solutions

Preservation solutions are used to maintain the hypothermic organ in optimal condition from the time of explantation until implantation

Organ Preservation Solutions

- Simple cooling with cold solution
- Continuous hypothermic perfusion
- Collins (1967)
- Euro-Collins (1980)
- University of Wisconsin - ViaSpan (1986)
- HTK - Custodiol (1980's)
- Celsior – 1994
- Polysol
- Normothermic perfusion

Euro-Collins Solution

- High potassium, glucose, and phosphate-based solution
- Designed to mimic composition of intracellular fluid
- Low cost
- Poor preservation quality
- Short preservation times achievable

UW Solution

- First developed for and applied in preservation of canine pancreas
- Use of impermeant molecules, lactobionate and raffinose, in preventing cell swelling
- Hydroxyethyl starch to minimize interstitial edema during machine perfusion, not necessary during cold storage
- High $[K^+]$, low $[Na^+]$

HTK Solution (Custodiol)

- Developed as cardioplegia
- Low potassium
- High buffering capacity of histidine
- **No colloid** - viscosity equal to that of pure water from 1 to 35°C, with mean flow rate 3x that of UW solution at equal perfusion pressure - organs exsanguinate and cool down to lower temperatures more rapidly than with UW

Optimal preservation times

	Euro Collins	Custodiol (HTK)	ViaSpan
Heart	4	8	4
Lung	6	6	8
Liver	8	12	12
Kidney	30	30	40
Pancreas	6	4	12
SB	4	4	8

In hours

Ischemic injury periods

- **Warm ischemia time 1 (WIT1)** -
from heart arresting to decreasing organ temperature to 4°C
mainly in NHBD
- **Cold ischemia time (CIT)**
time when organ is been cooled down to 4°C
– *transportation time and backtable preparations*
- **Warm ischemia time 2 (WIT 2)** - time of vascular anastomoses
- **Reperfusion**
- **Total ischemia time (TIT) – WIT1 + CIT + WIT2**

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Methods of preservation

Simple hypothermia (cold storage)

Continuous pulsatile perfusion in hypothermia

Simple hipotermia (cold storage)



Methods of preservation

Continuous pulsatile perfusion in hypothermia

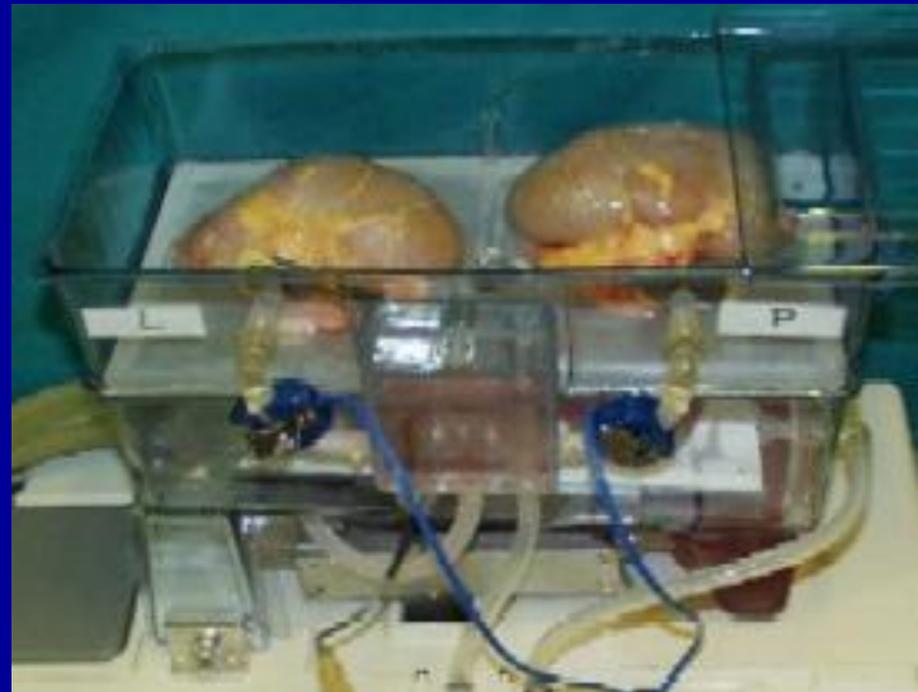
CPPH

Advantages

- better outcome after Tx
- good results with longer CIT
- improves intracellular metabolism
- improves kidney perfusion
- allows to monitor viability of kidney
- allows to predict kidney function after Tx
- allows to accept marginal donors

Restrictions

- higher costs
- pump damages



Continuous pulsatile perfusion in hypothermia



Organ Matching Criteria

- Medical urgency
- Tissue match
- Blood type
- Waiting time
- Organ size
- Immune status
- Geographic distance

Recipient selection process

- Location (local, regional, national)
- ABO blood type compatibility
- Severity of illness (**except kidneys and pancreas**)
- Length of time on waiting list (elective!)
- Histocompatibility leukocyte antigen (HLA) match (*pancreas, kidneys*)
- Degree of preformed antigen sensitivity (panel reactive antibody score -PRA, *kidneys only*)
- Other special factors (eg, pediatric patients in specific age categories, reciprocal sharing arrangements or pay back agreements, dual organ recipient, liver transplant for hepatic malignancy, acute failure of recent transplanted organ)