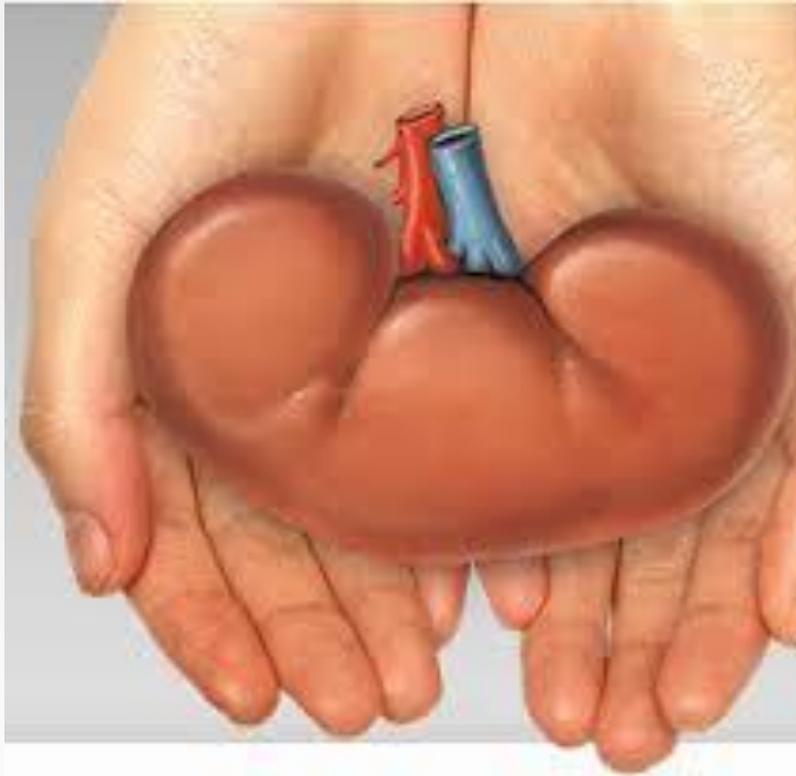


RENAL TRANSPLANTATION

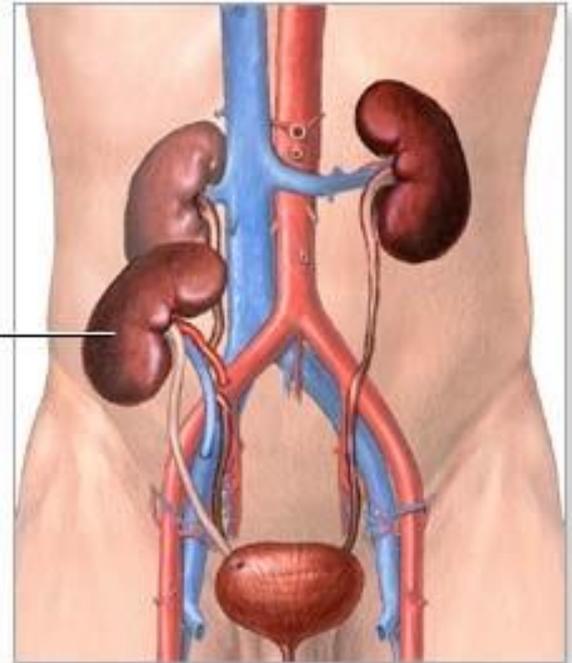


By
Dr. Duraid Al-Hadithi

- ◉ kidney transplantation is the pioneer discipline in solid organ transplantation.
- ◉ The relationship between transplant surgeon and nephrologist has served as a model for multidisciplinary team care.
- ◉ Understanding the molecular mechanisms of antigen-lymphocyte interactions in transplantation should provide insights into other disease processes such as cancer and infection.



Transplanted
kidney



END-STAGE RENAL DISEASE

Incidence and Prevalence

- The estimated number of patients starting renal replacement therapy each year for end-stage renal disease (ESRD) in the United States is about 360 per million population (2010).
- The median age of these new ESRD patients is 64 years.
- ESRD are more common in elderly than in young patients, in men than in women, and in African-Americans, Hispanics, and Native Americans than in Asians and whites.
- Diabetes mellitus is the most frequent cause of ESRD, followed in order by hypertension, glomerulonephritis, and renal cystic disease.
- The incidence of ESRD is greater than that for any urologic malignancy except prostate cancer, and more patients die annually from ESRD than from any urologic malignancy.

Treatment Options

- The purposes of renal replacement therapy are to prolong and maintain the quality of life.
- Permanent renal failure in adults is commonly defined as an irreversible glomerular filtration rate (GFR) of less than 10 mL/min or a serum creatinine level of greater than 8 mg/dL.
- The number of patients listed for kidney transplantation continues to expand disproportionately to the number of kidney transplantations performed annually.
- Hemodialysis is the predominant form of therapy for adults with ESRD. In the United States, it accounts for about two thirds of the treated ESRD patients.

Treatment Options

- Transplantation, however, is the predominant mode of care for patients younger than 20 years.
- About 10% of ESRD patients are treated with chronic peritoneal dialysis.
- **A desire for self-care, a long distance from a hemodialysis unit, difficulties with hemodialysis therapy, serious cardiac disease, diabetes mellitus, and small stature** are characteristics of patients especially suited for peritoneal dialysis.
- Unsuitable characteristics of patients for chronic peritoneal dialysis are considered to be **obesity, hernias, poor hygiene, inflammatory bowel disease, and obliterated peritoneal space.**
- The advantages of living related donor compared with deceased donor are **better probabilities of graft survivals, less recipient morbidity, specific planning of the operation to allow preemptive transplantation or limitation of the waiting time on dialysis.**

Treatment Options

- **that survival after renal transplantation is significantly better than that of patients treated with dialysis.**

HISTORY OF HUMAN RENAL TRANSPLANTATION

- In 1933 the first human renal allograft was performed by Voronoy in the Ukraine.
- The first long-term success with human renal allografting, in which the patient survived for over a year, occurred in Boston in 1954.
- In 1958 the first histocompatibility antigen was described.
- Radiation was used for immunosuppression in 1959.
- azathioprine became available for human use in 1951, and glucocorticoids became part of a standard immunosuppression regimen with azathioprine in 1962.
- In the same year, the first use of tissue matching to select donor-recipient pairs was done.
- In the late 1960s human renal preservation over 24 hours became possible with either pulsatile machine perfusion or simple cold storage after flushing with an ice-cold intracellular electrolyte solution.

HISTORY OF HUMAN RENAL TRANSPLANTATION

- The first clinical trials of cyclosporine were reported by Calne and colleagues in 1978.
- Laparoscopic donor nephrectomy was introduced in 1995 to reduce disincentives for living donor nephrectomy.
- First kidney transplant in Iraq at 1973.

SELECTION AND PREPARATION OF KIDNEY TRANSPLANT RECIPIENTS

The purposes of the evaluation are generally considered to be to diagnose the:

- ⦿ primary renal disease and its risk of recurrence in the kidney graft
- ⦿ to rule out active invasive infection,
- ⦿ a high probability of operative mortality,
- ⦿ noncompliance,
- ⦿ active malignancy, and unsuitable conditions for technical success.
- ⦿ Kidney Disease Recurrence Patients with **focal segmental glomerulosclerosis, hemolytic-uremic syndrome, and primary oxalosis** should be counseled about the significant probability of disease recurrence and the risk of secondary graft failure.

Check list for recipient

- Prior substance abuse?
- Morbid obesity body mass index of greater than 35.
- Compliance issues?
- High risk for heart disease
- Problem list
- Medication list
- Medical history
- Immunization history
- Physical exam
- Stool occult blood
- Pap smear (women)
- Chest x-ray
- Tuberculin test

Check list for recipient

- ECG.
- Abdominal ultrasound.
- Doppler study .
- CBC.
- Chem screen.
- INR, APTT.
- Infectious serologies.
- PSA (men >40).
- Urine analysis + culture.

Check list for recipient

- Mammogram (women >40 years)
- Eye exam (>50 diabetics)
- Dental exam
- Social service consult
- Dietary consult
- Patient and family education
- Financial counseling
- Histocompatibility testing

Urologic Evaluation

- Kidney Disease Recurrence
- Infection
- Active Malignancy(To reduce the risk of cancer recurrence, a waiting time of 2 to 5 cancer-free years from the time of the last cancer treatment has been recommended for patients who have had invasive malignancies).
- The purposes of the urologic evaluation are to determine the suitability of the urinary bladder or its substitute for urinary tract reconstruction and to determine the necessity for removal of the native kidneys before or at the time of renal transplantation.

DONOR SELECTION, PREPARATION, AND SURGERY

- The basic criteria for a renal donor are an **absence of renal disease**, **an absence of active infection**, and an **absence of transmissible malignancy**.
- the surgical goals are to minimize warm ischemia time, preserve renal vessels, and preserve ureteral blood supply. In the deceased donor, it is also necessary to obtain histocompatibility specimens and sometimes necessary to remove iliac vessels for vascular reconstruction of the donor kidney.

type of kidney donors

There are two type of kidney donors:

- Live donor (related and non related).
- Deceased donor (heart beating and non heart beating)

Deceased Donor

The declaration of brain death is the responsibility of the potential deceased organ donor's physician.

- **The criteria for an ideal deceased kidney donor are:**
- ⊙ normal renal function, no hypertension requiring treatment,
- ⊙ no diabetes mellitus.
- ⊙ no malignancy other than a primary brain tumor or treated superficial skin cancer.
- ⊙ no generalized viral or bacterial infection.
- ⊙ acceptable urinalysis.
- ⊙ age between 6 and 50 years.
- ⊙ and negative assays for syphilis, hepatitis, HIV, and human T-lymphoproliferative virus.

EVALUATION OF RENAL DONOR

- Education of potential donor(s) about risks and benefits.
- Medical history
- Medication list
- Blood pressure
- Recent physical exam results, if available
- Recent CBC, chemistry panel, UA if available
- ABO blood group, if available.
- Significant mental dysfunction?
- Renal disease?
- High risk for mortality or morbidity?
- Significant transmissible disease?

Types of kidney retrieval :

- ⦿ Laparoscopic (transperitoneal or retroperitoneal).
- ⦿ Robotic.
- ⦿ Open surgery.

After kidney retrieval

- ⦿ The back table to be used for renal perfusion is set up with slush in a pan, cold University of Wisconsin solution in a bag pressurized to 150 mm Hg, attached tubing with a vascular perfusion cannula.
- ⦿ The kidney is immediately delivered from the periumbilical incision, placed on slush, and flushed through the artery with cold reservation solution.



Clinical Kidney Transplant Preservation



Clinical Kidney Transplant Preservation

- The basic methods of kidney reservation are pulsatile machine perfusion with a protein-based solution and hypothermic flushing followed by simple cold storage.
- simple cold storage became more widely used for human kidney preservation.
- Machine perfusion has provided reliable human kidney preservation for up to 72 hours (Feduska et al, 1978), and it is becoming the preferred method of preserving kidneys.
- The commonly used **UW** solution minimizes cellular swelling with the impermeant solutes lactobionate, raffinose, and hydroxyethyl starch.

RENAL ALLOGRAFT REJECTION

- Protocols have been developed to use kidney transplants where the recipient has a positive cross match to the donor, and the cross match is rendered negative by plasmapheresis or immunoadsorption and immunoglobulin administration to permit an otherwise prohibited transplant to take place.

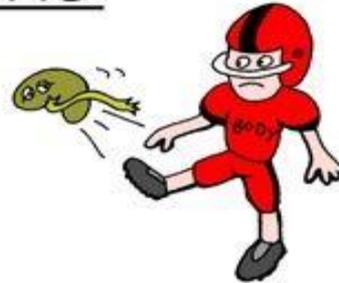
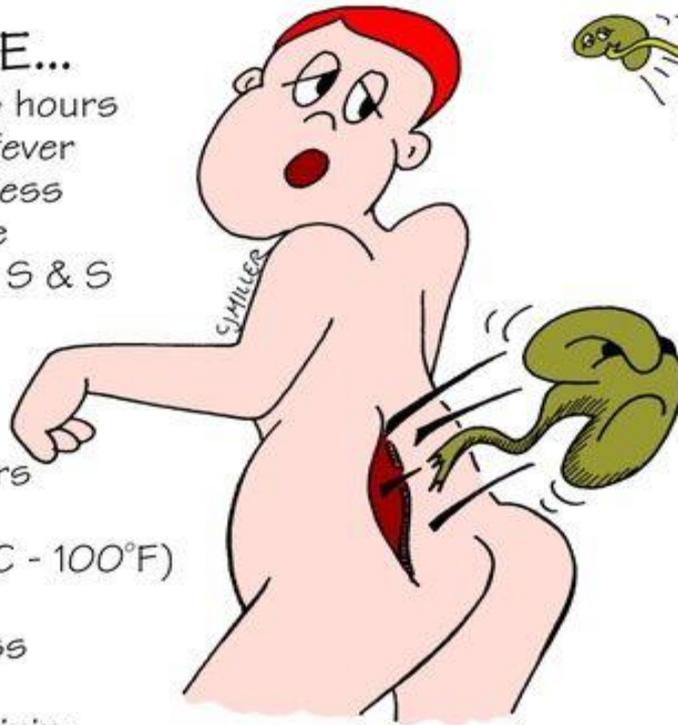
POST KIDNEY TRANSPLANT REJECTION SIGNS

HYPERACUTE...

- Onset with 48 hours
- Malaise, high fever
- Graft tenderness
- Organ must be removed to ↓ S & S

ACUTE...

- 1 Week to 2 Years
- Oliguria, Anuria
- ↑ Temp ($>37.8^{\circ}\text{C}$ - 100°F)
- ↑ BP
- Flank Tenderness
- Lethargy
- ↑ BUN, K, Creatinine
- Fluid Retention



CHRONIC...

- Gradual Over Months to Years
- ↑ In BUN, Creatinine
- Imbalances in Proteinuria Electrolytes
- Fatigue

Classification of Rejection

- **Hyperacute rejection** : occurs immediately after renal revascularization.
- It is an irreversible process mediated by preformed circulating cytotoxic antibodies that develop after pregnancy, blood transfusions, or an earlier failed transplantation.
- Hyperacute rejection is rare when the micro lymphocytotoxicity cross match between recipient serum and donor lymphocytes is negative.
- **Accelerated rejection**: is mediated by humoral and cellular components of the immune response. It occurs within days to weeks and often does not respond to anti rejection therapy.

- **Acute rejection** :can occur any time after transplantation. The symptoms of acute kidney transplant rejection are those of “the flu” accompanied by pain over an enlarged kidney graft, hypertension, decreased urinary output, fluid retention, increased serum creatinine levels, and radioisotope renography indicating decreased renal blood flow, glomerular filtration, and tubular function.
- **Chronic rejection:** is characterized by a gradual decline in renal function associated with interstitial fibrosis, vascular changes, and minimal mononuclear cell infiltration. A positive B-cell cross match or a positive flow cross match against donor B or T cells is considered to be predictive of chronic rejection and poorer long term graft survivals.

Immunosuppression

- Immunosuppressive drug regimens commonly include a **glucocorticoid** in combination with other drugs such as **cyclosporine** or **tacrolimus** (calcineurin inhibitors), **azathioprine** or **mycophenolate mofetil** (purine antagonists), and sometimes **antilymphocyte antibody preparations**.
- The most common maintenance immunosuppression is with a glucocorticoid, tacrolimus, and mycophenolate mofetil

Renal transplant PROBLEMS

Early Graft Dysfunction: can be due to:

- ⦿ Infection,
- ⦿ Renal allograft rejection,
- ⦿ Urinary or vascular obstruction,
- ⦿ Cyclosporine or tacrolimus nephrotoxicity,
- ⦿ Hyperglycemia,
- ⦿ Dehydration.

Renal transplant **PROBLEMS**

Vascular Complications:

- ⦿ Immediate vascular complications include kinking of the kidney graft's artery or vein, suture line stenosis, or thrombosis.
- ⦿ Thrombosis of the kidney graft may occur because of hyperacute rejection or thrombophilia.
- ⦿ Renal artery stenosis after renal transplantation is usually diagnosed because of hypertension that is progressively difficult to manage, with or without impaired renal function.

Renal transplant PROBLEMS

- **Medical Vascular Complications:** Nonsurgical hypertension after renal transplantation is common.
- Causes of this include medications (glucocorticoids, cyclosporine, and tacrolimus); intrinsic renal disease; and rejection.
- In spite of aggressive preoperative assessment and treatment, myocardial infarction and stroke continue to be leading causes of death in these patients.
- Prednisone and cyclosporine increase cardiovascular risk because of the hyperlipidemia associated with these drugs, and post-transplant hyperlipidemia should be treated aggressively with dietary changes and, if necessary, antilipid medications.

Renal transplant PROBLEMS

- **New Diabetes Mellitus:**
- New diabetes occurs in a significant percentage of kidney transplant recipients.
- **This is due to the diabetogenic effects of glucocorticoids and calcineurin inhibitors.**
- **The incidence of insulin-dependent post-transplant** diabetes mellitus is significantly higher in patients treated with tacrolimus than in those treated with cyclosporine.

Renal transplant PROBLEMS

Cancer:

- Kidney transplant recipients are more likely to develop cancer than age-matched subjects in the general population and patients wait-listed for deceased donor renal transplantation.
- This was especially true for Kaposi sarcoma, non- Hodgkin's lymphomas, non melanoma skin cancers, and kidney cancer.
- New evidence shows no increase in the incidence of prostate cancer after kidney transplantation.

