RENAL FAILURE & KIDNEY TRANSPLANT: HISTORY AND PROGRESS

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DISCLOSURE

• I have no financial relationship(s) relevant to the content of this CME activity.

• I will not discuss off-label use of medications.
RENAL FAILURE

- Definition: Failure of kidney to adequately filters blood from the waste products of metabolism.
- Types:
  - A) Acute Renal failure (usually reversible).
  - B) Chronic Renal failure (irreversible).
INCIDENCE & EPIDEMIOLOGY OF KIDNEY DISEASE

- One in 10 American, more than 20 million, have some level of CKD.
INCIDENCE RATE OF RENAL FAILURE IN THE USA.
INCIDENCE & EPIDEMIOLOGY OF KIDNEY DISEASE

Adjusted Incident Rates of ESRD by Race

Rate per Million

Year


African American
All
American Indian
Asian
Caucasian
OPTIONS FOR TREATING PATIENT WITH ESRD

• 1- DIALYSIS:
  - Hemodialysis or Peritoneal dialysis

• 2-KIDNEY TRANSPLANT:
  - Cadaveric or Live donor

• 3-DO NOTHING:
  = DEATH
HISTORY OF HEMODIALYSIS

• 1943: Dr. Willem Kolff built the first dialysis machine.
HISTORY OF HEMODIALYSIS
HISTORY OF HEMODIALYSIS

Figure 1. The first rotating artificial kidneys awaiting the end of the war to be sent to other countries. In the garden of the hospital at Kampen, September 1944.
HISTORY OF HEMODIALYSIS

“No man and no institution have done more for the propagation of dialysis in the United States than John P. Merrill and the Peter Bent Brigham Hospital”

DR. MURRAY
• 1960: Dr. Belding Scribner invent the first dialysis access.
WHO SHALL LIVE?
NBC news 1965
LIMITATION OF DIALYSIS

- COST: $87,945 PPPY for hemodialysis and $71,630 PPPY for peritoneal dialysis
FINANCIAL BURDEN

ESRD Costs in Billions

Year 1998 2000 2005 2009
Total Costs $16.74 $19.35 $31.99 $42.50

Non-Medicare Costs $4.70 $5.53 $10.68 $13.47
Medicare Costs $12.04 $13.82 $21.31 $29.03
FINANCIAL BURDEN

Annual ESRD Treatment Costs per Patient for HD, PD, Transplantation (Tx), and all ESRD

Cost

Year

2006  2007  2008  2009

HD  PD  Tx  All ESRD
Cumulative 1-year Savings: Renal Transplantation vs Dialysis

LIMITATION OF DIALYSIS

- COST; $87,945 PPPY for hemodialysis and $71,630 PPPY for peritoneal dialysis
- Vascular access problems.
- Impaired quality of life.
- Risk of disease transmission.
CAUSE OF MORTALITY ON DIALYSIS

- Cerebrovascular disease: 7%
- Infection: 20%
- Malignancy: 13%
- Other: 23%
- Cardiovascular disease: 37%

Cardiovascular Annual Mortality:
- General: 0.28%
- Hemodialysis: 9.12%
- Peritoneal dialysis: 9.24%
- Renal transplant: 0.54%

N=47,581

USRDS database, 2001
PATIENT SURVIVAL AFTER DIALYSIS AND KIDNEY TRANSPLANT

![Graph showing patient survival rates by dialysis and transplant](image)
**HISTORY OF KIDNEY TRANSPLANT**

- **1902:** The first successful experimental kidney transplants were performed at the Vienna Medical School in Austria with animals.
- **1933:** The first human renal transplant by Voronoy Soviet Surgeon. A 60 year old donor to a 26 year old recipient.
- **1950:** The first kidney transplantation was performed on, a 44-year-old woman with polycystic kidney disease, at Little Company of Mary Hospital in Evergreen Park, Illinois. Although the donated kidney was rejected ten months later.
- **1952:** The first kidney transplants between living patients were undertaken at the Necker hospital in Paris by Jean Hamburger although the kidney failed after 3 weeks of good function.
1954: The first successful kidney transplant between 2 twins by Dr. Murray.
Ten months after the transplant, Ronald Herrick (left) and his identical twin Richard toast their good health.
In July 2004, transplant pioneer Dr. Joseph Murray (left), 85, was reunited with his first organ donor, Ronald Herrick, 73, at the U.S. Transplant Games in Minneapolis. Richard Herrick died eight years after his kidney transplant.
OBSTACLES ON THE ROAD

- PRESERVATION
- SURGICAL MANIPULATION
- I/R INJURY
- CHRONIC REJECTION
- ACUTE REJECTION
- SEPSIS
CORNER STONE IN IMMUNOSUPPRESSION

Sir Peter Brian Medawar. Brazilian/British biologist, whose work on graft rejection and the discovery of acquired immune tolerance was fundamental to the practice of tissue and organ transplants. He was awarded the 1960 Nobel Prize in Physiology or Medicine.
CORNER STONE IN IMMUNOSUPPRESSION

• 1960: Schwartz and Dameshek in Boston developed a 6-Mercaptopurine analogue “Azathioprine”

• 1983: Cyclosporine was introduced as an effective antirejection medicine by Sir Roy Yorke Calne

• 1989: Fk506 (Tacrolimus) has been introduced by Thomas Starzle as a potent antirejection medicine.
CORNER STONE IN IMMUNOSUPPRESSION

1-Sir Roy Calne introduce CYCLOSPORINE IN 1970

2- Thomas Starzl introduce the FK506 (Prograf) in 1989
PRESERVATION SOLUTION

• The pioneering work by Collins and his colleagues led to the design of an acellular solutions termed (Collins solutions) In the mid 1960s.
• UW solution: Introduced by Belzer and coworkers in the mid 1980s.
• HTK solution: was introduced in late 1990s.
INDICATIONS FOR KIDNEY TRANSPLANTATION

• IRREVERSIBLE END STAGE RENAL DISEASE REQUIRING OR APPROACHING THE NEED FOR RENAL REPLACEMENT THERAPY
INDICATIONS FOR KIDNEY TRANSPLANTATION

- **Glomerulonephritis**
- Idiopathic and post infectious crescentic
- Membranous
- Mesangiocapillary (Type I)
- **Mesangiocapillary** (Type II) (dense-deposit disease)
- IgA nephropathy
- Antiglomerular basement membrane
- Focal glomerulosclerosis
- Henoch-Schönlein
- Chronic pyelonephritis (reflux nephropathy)
- **Metabolic**
  - Diabetes mellitus
  - Hyperoxaluria
  - Cystinosis
  - Fabry's disease
  - Amyloid
  - Gout
  - Porphyria
  - **Obstructive nephropathy**
  - **Toxic**
    - Analgesic nephropathy
    - Opiate abuse
- **Hereditary**
  - Polycystic kidneys
  - Nephronophthisis (medullary cystic disease)
  - Nephritis (including Alport's syndrome)
  - Tuberous sclerosis
INDICATIONS FOR KIDNEY TRANSPLANTATION

- **Multisystem Diseases**
  - Systemic lupus erythematosus
  - Vasculitis
  - Progressive systemic sclerosis

- **Haemolytic uraemic syndrome**

- **Tumors**
  - Wilms' tumor
  - Renal cell carcinoma

- **Incidental carcinoma**
- **Myeloma**

- **Congenital**
  - Hypoplasia
  - Horseshoe kidney

- **Irreversible Acute Renal Failure**
  - Cortical necrosis
  - Acute tubular necrosis
INDICATIONS FOR KIDNEY TRANSPLANTATION

THE CHIEF CAUSES OF ESRD IN CHILDREN ARE:

• Obstructive uropathy
• Hypoplastic or dysplastic kidneys
• Reflux nephropathy
• Focal segmental glomerulosclerosis as a variant of childhood nephritic syndrome
• Polycystic kidney disease, autosomal-recessive and autosomal-dominant varieties
INDICATIONS FOR KIDNEY TRANSPLANTATION

THE CHIEF CAUSES OF ESRD IN ADULTS ARE:

1- Diabetic nephropathy
2- Hypertensive nephropathy
3- Glomerulonephritis
4- Others
CONTRAINDICATIONS FOR KIDNEY TRANSPLANTATION

• ABSOLUTE CONTRAINDICATIONS FOR KIDNEY TRX:
  – Active infection
  – Active malignancy
  – Active drug use, alcoholism, or psychosis.
  – Medical noncompliance
  – BMI > 40.
  – Anatomy that makes transplantation technically impossible
CONTRAINDICATIONS FOR KIDNEY TRANSPLANTATION

- Severe pulmonary hypertension.
- Severe cardiopulmonary disease
- Liver cirrhosis with portal hypertension
- AIDS (positive HIV)
CONTRAINDICATIONS FOR KIDNEY TRANSPLANTATION

RELATIVE CONTRAINDICATIONS FOR KIDNEY TRANSPLANTATION:

• A. Significant cardiac disease
• B. Significant pulmonary disease
• C. Significant gastrointestinal disease
• D. Severe vascular disease: coronary, cerebral or peripheral
• E. Renal disease with significant potential for recurrence causing kidney graft loss
CONTRAINDICATIONS FOR KIDNEY TRANSPLANTATION

• F. Potential for noncompliance
• H. BMI > 35
• I. Age greater than 70 years
• G. Psychosocial/financial issues causing an inability to achieve adequate post-transplant care
• K. History of cancer.
PROCESS OF EVALUATION AND LISTING

1. Referral received
2. Coordinator review referral packet
3. Get authorization
4. Schedule ICV
5. Go to surgery or end referral
6. Start evaluation or end referral
7. Seen in clinic for surgery appt.
8. List, Differ, or ineligible
9. Present at selection committee
10. Receive evaluation testing
SELECTION COMMITTEE

ESSENTIAL MEMBERS

- Transplant Surgeon
- Transplant Nephrology
- Pre-transplant Coordinator
- Post-transplant Coordinator
- Social Worker
- Financial Specialist
- Transplant pharmacist
- Transplant/ Hospital administrator

OPTIONAL

- Psychology
- ID
- Cardiology
- Anesthesia.
SURGERY
IMMUNOSUPPRESSION

INDUCTION THERAPY:
- Thymoglobulin
- Atgam
- Basiliximab (Simulect)
- Alemtuzumab (Campath)
- OKT3

MAINTAINANCE THERAPY:
- Prograf (Tacrolimus)
- Cyclosporine (Neoral)
- Rapa-immune.
- Imuran
- Prednisone.
- Cellcept (MMF)
IMMUNOSUPPRESSION


Graft Survival, %

No DGF

DGF, acute rejection

CsA+AZA

CsA+MMF

TAC+AZA

TAC+MMF

90.5

91.4

92.1

92.4

80.2

82.1

83.5

83.9

DGF = delayed graft failure
COMPLICATIONS AFTER KIDNEY TRANSPLANT

• Early Graft dysfunction:
  – Primary non-function (PNF)
  – Delayed graft function (DGF)
  – Vascular thrombosis

• Rejection
KIDNEY REJECTION

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°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

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HYPERACUTE REJECTION
KIDNEY REJECTION

POST KIDNEY TRANSPLANT REJECTION SIGNS

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CHRONIC...
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COMPLICATIONS AFTER KIDNEY TRANSPLANT

• Graft dysfunction:
  – Primary non-function (PNF)
  – Delayed graft function (DGF)
  – Vascular thrombosis

• Rejection

• Infection

• High Blood Pressure

• Post-Transplant Diabetes

• Lymphocele

• Disease recurrence.
Diseases which may recur in renal transplants are listed below:
- IgA nephropathy
- Focal segmental glomerulosclerosis
- Membranous glomerulonephritis
- Membranoproliferative glomerulonephritis
- Amyloidosis
- Cystinosis
CAUSE OF MORTALITY

Causes of Mortality in Kidney Transplant Patients

N=47,581

- Cerebrovascular disease: 7%
- Infection: 20%
- Malignancy: 13%
- Cardiovascular disease: 37%
- Other: 23%

USRDS database
ORGAN SHORTAGE

• Every ten minutes, someone is added to the national transplant waiting list.

• On average, 21 people die each day while waiting for a transplant.
ORGAN SHORTAGE

Renal Transplantation as Therapy for End Stage Renal Disease
2000 - 2009

INCREASE IN THE WAITING LIST TIME

KI 1.11 Median years to kidney transplant for wait-listed adult patients
EFFECT OF PROLONGED WAITING TIME BEFORE TRANSPLANT

KI 1.10 Three-year outcomes for adult patients waiting for a kidney transplant among new listings in 2009

- Removed from list
- Died
- Transplanted (LD)
- Transplanted (DD)
- Still waiting

Months post-listing

Percent
HOW WE CAN NARROW THE GAP?

1- Increasing the donor pool:
   - public education
   - Educate health care professionals
   - expanding donor criteria
   - New organ allocation system.

2- Increase longevity of the graft:
   - refinement of surgical techniques
   - refinement of immunosuppression

3- xenotransplantation: -

4- Increasing live donation:
ADVANTAGES OF LIVE KIDNEY DONOR TRANSPLANT

- Improved patient and graft survival
- Avoids prolonged time on the waiting list
- Elective surgery
- Decreased incidence of delayed function
- Decreased costs
- Increases the organ supply
ADVANTAGES OF LIVE KIDNEY DONOR TRANSPLANT
EFFECT OF PROLONGED WAITING TIME AFTER TRANSPLANT

Ten Year Overall Adjusted Graft Survival
Pre-emptive Living Donor Transplant vs. Dialysis

- Pre-Emptive Transplant: 75%
- After 24 Months on Dialysis: 49%

*Source: Meier-Kriesch HU, Kaplan E., Transplantation, 2002 Nov 27; 74(10): 1377-81
DISINCENTIVES TO LIVE DONATION

Prolonged convalescence.

Fear of pain

Cosmetic concerns

• 2013 Living Donor Age Breakdown:
  • Ages 18-34: 29.8%
  • Ages 35-49: 40.9%
  • Ages 50-64: 27.2%
  • Age 65+: 2.1%

• 2013 Living Donor Gender Breakdown:
  • Male: 38.6%
  • Female: 61.4%
OPEN DONOR NEPHRECTOMY
MINIMAL INVASIVE PROCEDURE

- Revolution over the past 2 decades
- Applied to a myriad of procedures
- Decreased hospital stays
- Decreased post-operative pain
- Decreased recuperative times
- Improve cosmetic outcome
1995 Ratner et al.

- First Laparoscopic donor nephrectomy

TYPES OF MINIMAL INVASIVE SURGERY FOR DONOR NEPHRECTOMY

• Total laparoscopic donor nephrectomy
• Hand assisted laparoscopic donor nephrectomy
• SILS Trans-umbilical laparoscopic donor nephrectomy
• Trans-vaginal laparoscopic donor nephrectomy.
• Robotic donor nephrectomy
PATIENT SELECTION

• All candidates for living kidney donation are potential for the laparoscopic nephrectomy

• Relative contraindications:
  – Previous abdominal surgery
  – Abnormal renal anatomy
  – BMI?

• Radiological Evaluation of the Renal Anatomy
  – Standard angiography with IVP
  – “State of the Art” 3D CT reconstruction
THE 3D CT
THE 3D CT
THE 3D CT
THE 3D CT
THE PROCEDURE

Donor Nephrectomy
10 DAYS POST LAPAROSCOPIC DONOR NEPHRECTOMY
10 DAYS POST LAPAROSCOPIC DONOR NEPHRECTOMY
Does kidney donation affect the life expectancy of the donor?

- Interestingly, people who have donated a kidney outlive the average person. (Reference: Fehrman-Ekholm, Ingela 2,3; Transplantation, 64(7): 976-978, October 15, 1997.)

- Donating a kidney is major surgery but does not reduce a person's life expectancy.
ESRD PATIENTS BY TREATMENT MODALITIES

Number of ESRD Patients by Treatment Modality

- Transplant Patients (172,553)
- Dialysis Patients (398,881)
- Other or uncertain dialysis (1,262)
- Continuous cycler-assisted peritoneal dialysis (18,064)
- Continuous ambulatory peritoneal dialysis (9,458)
- Home HD (4,511)
- In-center HD (365,566)
CURRENT STATUS OF KIDNEY TX.

WAITING LIST CANDIDATES

- All 123,448
- Kidney 101,748
- Pancreas 1,078
- Kidney/Pancreas 2,012
- Liver 15,290
- Intestine 247
- Heart 4,103
- Lung 1,606
- Heart/Lung 38
KIDNEY TRANSPLANT IN THE US

Annual Number of Kidney Transplants

- Total
- Deceased Donor
- Living Donor

Number

10,000

5,000

0

Year

TYPES OF KIDNEY DONATION

1- Directed Kidney donation
2- Paired kidney donation
3- Samaritan kidney donation
PAIRED KIDNEY DONATION
KIDNEY CHAIN DONATION
ADVANTAGES OF KIDNEY TRANSPLANT VIA NKR

Graft Survival
NKR Transplants vs. U.S. Living Donor Transplants

*Source: Kaplan-Meier GS calculations provided courtesy of UCLA Department of Nephrology and Urology as of 3/21/14*
NEW KIDNEY ALLOCATION SYSTEM (KAS)

- WAITING TIME
- KDPI
- EPTS
- DEGREE OF SENSITIZATION
- PEDIATRIC PATIENTS
- EARLY REFERRAL TO TRANSPLANT
FUTURE OF KIDNEY TX.

- More improvement in immunosuppression.
- Desensitization of recipient with high PRA.
- Organ shortage.
- Expanding of PKD and NKR.
- Xenotransplantation.

Never ever give up!
KIDNEY TRANSPLANT STAND THE TEST OF TIME

SOME THINGS COME AND GO AND OTHERS STAND THE TEST OF TIME
CONCLUSION

• Major achievements in treating patient with Renal failure occurred during the past century.

• The major corner stones in kidney transplant were the development of antirejection medicine, preservation solution, and surgical techniques.

• Kidney transplant proved to be superior to dialysis both in cost, patient quality of life and patient survival.
CONCLUSION

• LDN with its advantages of less pain, shorter hospitalization, minimal scarring, and quicker recuperation increased the number of individuals willing to donate.

• The future will depend on more refinement of immunosuppression, expansion of shared donation and more research in the field of xenotransplantation.
QUESTION?

ONE OF THESE TWO WILL GET YOUR ORGANS.
YOU DECIDE.
Centers performing adult kidney transplants in 2012, within Donation Service Areas (DSAs)