

RETRANSPLANTATION FOLLOWING REJECTION AND RECURRENT DISEASE

RICHARD N FINE MD

PROFESSOR OF PEDIATRICS

STONY BROOK UNIVERSITY SCHOOL OF MEDICINE

STONY BROOK, NEW YORK

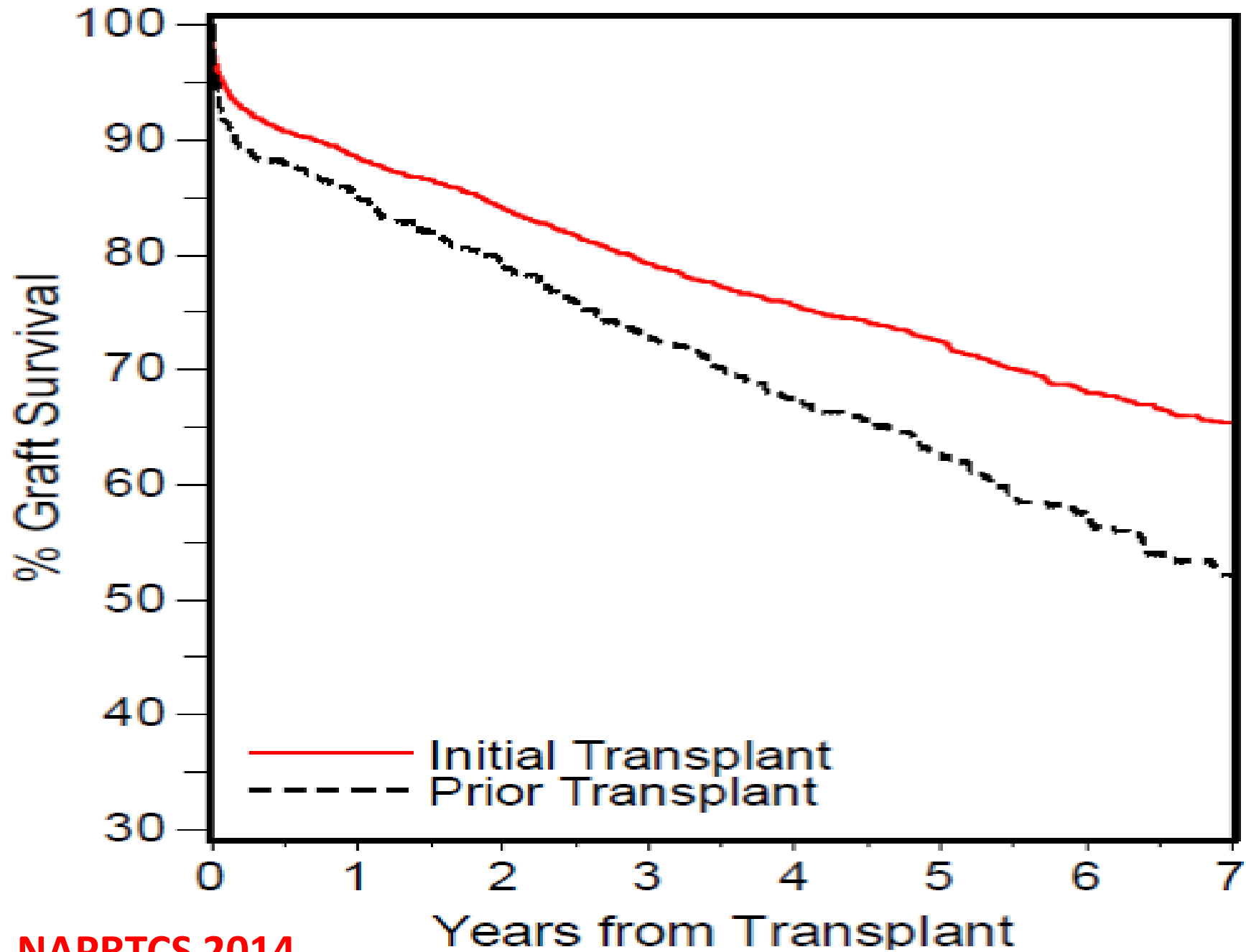
RETRANSPLANTATION

- **WHY IS RETRANSPLANTATION BECOMING AN INCREASING CLINICAL CHALLENGE?**
 - **INCREASING NUMBERS OF PATIENTS ON THE DECEASED DONOR WAIT LIST ARE AWAITING A RETRANSPLANT**
 - **± 15% OF CURRENT ANNUAL TRANSPLANTS IN THE UNITED STATES ARE RETRANSPLANTS**
 - **PEDIATRIC RECIPIENTS WILL LIKELY REQUIRE A RETRANSPLANT IN THEIR LIFETIME**

RETRANSPLANTATION

- **WHAT IS THE CURRENT OUTCOME OF KIDNEY RETRANSPLANTATION COMPARED TO THAT OF THE INITIAL KIDNEY TRANSPLANT?**

Transplant History



RETRANSPLANTATION: COMPARISON OF PRIMARY AND SUBSEQUENT GRAFT FAILURE RATES (NAPRTCS)

LIVE RELATED DONOR (N=5819)

DECEASED DONOR (N=5298)

TOTAL FAILURE 5YR*

TOTAL FAILURE 5YR*

% % %

% % %

NO PRIOR 88.7 19.1 83
TRANSPLANT

NO PRIOR 83 27 73
TRANSPLANT

PRIOR 11.3 28.1 81
TRANSPLANT

PRIOR 17 38 63
TRANSPLANT

*** SURVIVAL RATE**

RETRANSPLANTATION

- **WHAT ARE THE INITIAL KIDNEY GRAFT SURVIVAL RATES IN PEDIATRIC RECIPIENTS COMPARED TO THAT OF RETRANSPLANTS?**
 - **14,799 INITIAL KIDNEY GRAFTS IN PEDIATRIC (<18 YEARS OF AGE) RECIPIENTS IN THE *SRTR* DATABASE BETWEEN 1987 AND 2010**
 - **11,717 ONE TRANSPLANT (79.2%)**
 - **2634 TWO TRANSPLANTS (17.8%)**
 - **400 THREE TRANSPLANTS (2.7%)**
 - **46 FOUR TRANSPLANTS (0.3%)**

RETRANSPLANTATION

GRAFT #	SURVIVAL RATE (YEARS)		
	1	5	10
1	91.9%	74.8%	56.1%
2	89.3%	65.3%	43.9%
3	89.6%	62.0%	39.1%
4	84.9%	46.8%	19.5%

VAN ARENDONK ET AL 96:487, 2013

RETRANSPLANTATION

- **WHAT ARE THE ISSUES THAT COULD POTENTIALLY INFLUENCE THE OUTCOME OF KIDNEY RETRANSPLANTATION?**

RETRANSPLANTATION

- **ETIOLOGY OF INITIAL (OR SUBSEQUENT) KIDNEY GRAFT FAILURE?**
- **SHOULD THE FAILED KIDNEY GRAFT BE REMOVED PRIOR TO RETRANSPLANTATION?**
- **ARE THERE MITIGATING TECHNICAL CIRCUMSTANCES IMPACTING RETRANSPLANTATION?**
- **DID THE INITIAL (OR SUBSEQUENT) KIDNEY GRAFT FAIL FROM RECURRENCE OF THE PRIMARY KIDNEY DISEASE INVOLVING THE NATIVE KIDNEY?**

RETRANSPLANTATION

- **ARE THERE ETHICAL CONCERNS REGARDING OFFERING A SECOND OR SUBSEQUENT GRAFT TO A RECIPIENT WHO HAS HAD ONE OR MORE PRIOR GRAFTS IN LIGHT OF THE EVER EXPANDING WAIT LIST FOR AN INITIAL KIDNEY GRAFT?**
- **DOES THE CAUSE (?NON-ADHERENCE) OF THE INITIAL OR SUBSEQUENT GRAFT FAILURE RAISE FURTHER ETHICAL CONCERNS?**

RETRANSPLANTATION

- **HOW DOES THE CAUSE OF THE INITIAL (OR SUBSEQUENT) KIDNEY GRAFT FAILURE INFLUENCE RETRANSPLANTATION?**

RETRANSPLANTATION

- **ACUTE ANTIBODY MEDIATED REJECTION**
 - **%PRA (PANEL REACTIVE ANTI-HLA ANTIBODIES)**
 - **DSA (DONOR SPECIFIC ANTIBODIES)**
 - **OTHER (e.g. ANTI-ENDOTHELIAL ANTIBODIES, ANTI-MICA ANTIBODIES)**
- **CHRONIC ALLOGRAFT NEPHROPATHY (IF/TA)**
 - **LENGTH OF TIME OF INITIAL (OR SUBSEQUENT) KIDNEY GRAFT SURVIVAL**

RETRANSPLANTATION

- **THROMBOEMBOLIC PHENOMENON**
 - DOES AN UNDIAGNOSED HEREDITARY CLOTTING DISORDER EXIST?
- **INFECTION**
 - POLYOMA VIRUS (BK)
 - EPSTEIN-BARR (EBV) VIRUS – (?PTLD)
 - CYTOMEGALOVIRUS (CMV)

RETRANSPLANTATION

- **RECURRENCE IN THE GRAFT OF THE PRIMARY KIDNEY DISEASE CAUSING CHRONIC KIDNEY DISEASE IN THE NATIVE KIDNEYS**
 - WILL IT RECUR IN THE RETRANSPLANT?
- **NON-ADHERENCE**
 - WHAT IS THE INCIDENCE OF RECIDIVISM?
- **TECHNICAL MISHAP**

RETRANSPLANTATION

- **WHAT IS THE CURRENT RATE OF RETRANSPLANTATION FOLLOWING A FIRST AND/OR SECOND KIDNEY GRAFT FAILURE IN PEDIATRIC (<18 YEARS OF AGE) RECIPIENTS IN THE UNITED STATES?**

RETRANSPLANTATION

- 14,799 PEDIATRIC PATIENTS RECEIVED AN INITIAL KIDNEY TRANSPLANT IN THE *SRTR* (SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS) BETWEEN 1987 AND 2010
 - 5772 FIRST KIDNEY GRAFTS FAILED
 - 1158 SECOND KIDNEY GRAFTS FAILED

RETRANSPLANTATION

- 50.4% OF THE RECIPIENTS RECEIVED A RETRANSPLANT AND 12.1% DIED WITHIN 5 YEARS AFTER FAILURE OF THE FIRST TRANSPLANT
- 36.1% OF THE RECIPIENTS RECEIVED A RETRANSPLANT AND 15.4% DIED WITHIN 5 YEARS AFTER FAILURE OF A SECOND TRANSPLANT

VAN ARENDONK ET AL TRANSPLANTATION 95:1630, 2013

RETRANSPLANTATION

- **THEREFORE, A SIGNIFICANT NUMBER OF PEDIATRIC PATIENTS WERE NOT CANDIDATES FOR IMMEDIATE (WITHIN 5 YEARS) RETRANSPLANTATION FOLLOWING AN INITIAL OR SUBSEQUENT KIDNEY GRAFT FAILURE!**
- **WHAT ARE THE REASONS?**

RETRANSPLANTATION

- **FACTORS RELATED TO THE DECREASED RATE OF RETRANSPLANTATION**
 - **OLDER AGE @ TIME OF KIDNEY GRAFT FAILURE**
 - **MINORITY RACE**
 - **PUBLIC INSURANCE**
 - **ELEVATED PEAK %PRA (PANEL REACTIVE ANTIBODIES)**
 - **EARLIER INITIAL KIDNEY GRAFT FAILURE**

RETRANSPLANTATION

- **WHAT ARE THE INDICATIONS FOR FAILED KIDNEY GRAFT NEPHRECTOMY PRIOR TO RETRANSPLANTATION?**

RETRANSPLANTATION

- **CENTER PROTOCOL**
 - **CHRONIC INFLAMMATORY RESPONSE SYNDROME (GRAFT INTOLERANCE SYNDROME)**
 - **↑ CRP/ESR**
 - **ESA (ERYTHROPOETIN) RESISTENCE**
 - **HYPOALBUMINEMIA**
 - **MALNUTRITION**
- **MAKE ROOM FOR A RETRANSPLANTED KIDNEY**

RETRANSPLANTATION

- **CLINICAL INDICATIONS**
 - **FEVER**
 - **GRAFT TENDERNESS**
 - **HEMATURIA**
 - **URINARY TRACT INFECTION**
- **↓ POLYOMA VIRUS (BK) LOAD**
- **PRESENCE OF (OR POTENTIAL FOR) TUMOR IN THE FAILED GRAFT**

RETRANSPLANTATION

- **POTENTIAL FOR THE RETAINED GRAFT TO DECREASE THE QUALITY OF LIFE AND CLINICAL STATUS DURING DIALYSIS**
- **CONTINUED IMMUNOSUPPRESSION REQUIRED TO SUPPRESS REACTIVITY OF THE RETAINED FAILED GRAFT**

RETRANSPLANTATION

- WHAT ARE THE RISKS TO NEPHRECTOMY OF A FAILED GRAFT PRIOR TO RETRANSPLANTATION?
 - MORBIDITY AND MORTALITY FROM THE SURGICAL PROCEDURE
 - ↑ %PRA (*PANEL REACTIVE ANTIBODIES*)/ DSA (*DONOR SPECIFIC ANTIBODIES*)
 - RETAINED GRAFT ABSORBS (FIXES) PRA/DSA
 - RETAINED GRAFT STIMULATES PRA/DSA

RETRANSPLANTATION

- **DOES A FAILED GRAFT NEPHRECTOMY ADVERSELY INFLUENCE RETRANSPLANT GRAFT SURVIVAL RATES?**
 - **ADULT DATA CONTRADICTORY**
 - **ONLY PEDIATRIC DATA INDICATED GRAFT NEPHRECTOMY ASSOCIATED WITH ↑HLA ANTIBODY LEVELS – NO SURVIVAL DATA PROVIDED (MINSON ET AL PEDIATR NEPHROL 28:1299, 2013)**

RETRANSPLANTATION

- **ARE THERE MITIGATING TECHNICAL CIRCUMSTANCES THAT IMPACT RETRANSPLANTATION?**
 - **VASCULAR THROMBOSIS**
 - **THROMBOSED IVC (INFERIOR VENA CAVA)**
 - **BLADDER DYSFUNCTION**

RETRANSPLANTATION

- DOES THE ORDER OF DONOR TYPE (*LRD* – LIVE RELATED DONOR vs *DD* – DECEASED DONOR) IMPROVE THE SUCCESS RATE FOLLOWING RETRANSPLANTATION?

RETRANSPLANTATION

- **VAN ARENDONK ET AL (TRANSPLANTATION 96:478, 2013) ANALYZED OUTCOMES OF FIRST AND SECOND TRANSPLANTS OF 14,799 PEDIATRIC RECIPIENTS IN THE *SRTR* DATABASE BETWEEN 1987 AND 2010**
 - ***LRD* 1ST AND 2ND GRAFTS HAD ↑ SURVIVAL RATE COMPARED TO 1ST AND 2ND *DD* GRAFTS**
 - **CUMMULATIVE SURVIVAL OF TWO GRAFTS WAS SIMILAR REGARDLESS OF ORDER OF THE TRANSPLANT DONOR TYPE**

RETRANSPLANTATION

- **WHAT IS THE IMPACT OF *HLA* MISMATCH ON SENSITIZATION AND SUBSEQUENT RETRANSPLANT GRAFT SURVIVAL RATES AFTER INITIAL GRAFT FAILURE IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS?**
 - IN *SRTR* DATABASE 11,916 PEDIATRIC RECIPIENTS RECEIVED A RENAL TRANSPLANT BETWEEN 1990 AND 2008
 - 2704 FAILED AND 1847 RECEIVED RETRANSPLANTS

RETRANSPLANTATION

- **TWO *DR* MISMATCHES IN THE INITIAL TRANSPLANT WAS ASSOCIATED WITH THE FOLLOWING IN RECIPIENTS WITH A FAILED GRAFT:**
 - **↑ *HLA* SENSITIZATION (%PRA)**
 - **↑ WAITING TIME FOR A 2ND GRAFT**
 - **↓ RATE OF 2ND TRANSPLANTATION (↓ BY 20%)**
 - **↓ REGRAFT SURVIVAL RATE**
 - **5 YR GRAFT SURVIVAL RATE ASSOCIATED WITH NUMBER OF 1ST AND 2ND GRAFT *DR* MISMATCHES**

RETRANSPLANTATION

- **WHAT IS THE RISK OF RETRANSPLANTATION FOLLOWING KIDNEY GRAFT LOSS FROM *BK* POLYOMA VIRUS NEPHROPATHY (*BKVN*)?**
 - **HIRSCH AND RANDHAWA AJT 13:179, 2013**
 - **DHARNIDHARKA ET AL AJT 10:1312, 2010**

RETRANSPLANTATION

- **SINGLE CENTER REPORTS 2004-2008**
 - 90% GRAFT AND PATIENT SURVIVAL IN 22 CASES OF RETRANSPLANTATION AFTER *BKVN*
 - 16/22 UNDERWENT GRAFT NEPHRECTOMY
 - 3/22 RECURRENCE OF *BKVN* AND 1/3 HAD GRAFT LOSS
- **OPTN DATABASE 6/04 – 12/08**
 - 126/823 *BKVN* GRAFT LOSSES RETRANSPLANTED
 - 118/126 (93.7%) FUNCTIONING AS OF 6/09
 - 1 GRAFT LOST TO *BKVN* AND 17.5% RxE D FOR *BKV*
- **RETRANSPLANTATION AFTER *BVKN* APPEARS TO ASSOCIATED WITH GOOD RESULTS**

RETRANSPLANTATION

- **UNANSWERED ISSUES REGARDING RETRANSPLANTATION FOLLOWING *BKVN***
 - **IS TRANSPLANT NEPHRECTOMY MANDATORY?**
 - **IS A ZERO VIRAL LOAD (BLOOD/URINE) REQUIRED PRIOR TO RETRANSPLANTATION?**
 - **WHAT IS THE OPTIMAL TIME INTERVAL BETWEEN INITIAL GRAFT FAILURE AND RETRANSPLANTATION?**

RETRANSPLANTATION

- **WHAT IS THE RISK OF RECURRENCE OF POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDERS (*PTLD*) FOLLOWING RETRANSPLANTATION?**
 - **JOHNSON ET AL AJT 6:2743, 2006**

RETRANSPLANTATION

- USING *UNOS* DATA BASE FROM 1987 – 2004
 - 27 KIDNEY RECIPIENTS (12 [44.4%] <18 YRS OLD) WHO LOST A GRAFT FOLLOWING *PTLD* WERE RETRANSPLANTED
 - MEDIAN TIME FROM *PTLD* DIAGNOSIS AND RETRANSPLANT WAS 1337 DAYS
 - 24/27 (88.9%) WERE ALIVE WITH A MEAN OF 742±107 DAYS
 - THERE WAS NO RECURRENCE OF *PTLD*

RETRANSPLANTATION

- **DOES A HISTORY OF NON-ADHERENCE IN A PRIOR KIDNEY TRANSPLANT RECIPIENT IMPACT ON THE INCIDENCE AND/OR RAPIDITY OF RETRANSPLANTATION IN THE RECIPIENT?**
- **WHAT IS THE INCIDENCE OF RECIDIVISM OF NON-ADHERENCE FOLLOWING KIDNEY RETRANSPLANTATION AND DOES IT IMPACT SUBSEQUENT GRAFT OUTCOME?**

RETRANSPLANTATION

- **NON-ADHERENCE**

- **HYMES ET AL (PEDIATR TRANSPLANT - IN PRESS)**
EVALUATED FACTORS PREDICTIVE OF RECEIVING A 2nd
TRANSPLANT AFTER A FAILED RENAL TRANSPLANT IN
51 CHILDREN WHO SUFFERED GRAFT LOSS BETWEEN
2003 -2011

- **21/51(41%) RECEIVED A 2nd TRANSPLANT WITHIN**
2 TO 81 MONTHS
- **NON-ADHERENCE WITH MEDICATIONS WITH THE**
INITIAL GRAFT WAS A SIGNIFICANT FACTOR IN
FAILURE TO RECEIVE A SECOND TRANSPLANT

RETRANSPLANTATION

- **NON-ADHERENCE (NA)**
 - **35 KIDNEY TRANSPLANT RECIPIENTS UNDERWENT RETRANSPLANTATION AFTER THOROUGH REEVALUATION**
 - **AT 8 YRS POST-TRANSPLANT THERE WAS NO DIFFERENCE IN PATIENT AND GRAFT SURVIVAL RATES, RENAL FUNCTION, OR BIOPSY-PROVEN CHRONIC REJECTION COMPARED TO A CONTROL GROUP OF NON-NON-ADHERENT (NNA) RETRANSPLANT RECIPIENTS**

RETRANSPLANTATION

- **NON-ADHERENCE**

- 14% OF **NA** GROUP COMPARED TO 2% OF **NON-NA** LOST THE RETRANSPLANT TO **NA** (p=0.0001)
- 57% OF **NA** GROUP EXHIBITED REPEAT **NA** AFTER RETRANSPLANT
- PRIOR **NA** SHOULD NOT BE A CONTRAINDICATION TO RETRANSPLANTATION

RETRANSPLANTATION

- DOBBELS ET AL (PEDIATR TRANSPL 16:4,2012) REVIEWED THE LITERATURE ON NON-ADHERENCE AND RETRANSPLANTATION AND IDENTIFIED ONLY THE REPORT BY DUNN ET AL.
- THE AUTHORS DISCUSSED ARGUMENTS FOR AND AGAINST RETRANSPLANTATION IN THE NON-ADHERENT RECIPIENT WITHOUT COMPELLING EVIDENCE TO SUPPORT EITHER POSITION
- THEY CONCLUDED “MEASUREMENT BEING THE FIRST STEP THAT LEADS TO CONTROL AND EVENTUALLY TO IMPROVEMENT. IF YOU CAN’T MEASURE IT ____ “

RETRANSPLANTATION

- **WHAT IS INCIDENCE OF GLOMERULAR DISEASES THAT COULD POTENTIALLY RECUR IN THE TRANSPLANTED KIDNEY?**
- ***NAPRTCS* 2014 (N=11,186)**

RETRANSPLANTATION

FSGS	1308	IgA VASCULITIS (HSP)	115
CHRONIC GN	344	MPGN TYPE II	87
CONGENITAL NS	289	WEGENER'S(POLYANGITIS	
HUS	288	/GRANULOMATOSIS)	71
IDIOPATHIC RPGN	195	MEMBRANEOUS GN	51
MPGN TYPE I	191	OTHER IMMUNOLGIC	34
SYSTEMIC LE	172	MEDIATED DISEASES	

RETRANSPLANTATION

- WHAT IS THE ACTUAL NUMBER OF GRAFTS THAT HAVE FAILED FROM RECURRENCE IN THE MOST RECENT **NAPRTCS** REPORT (2014)?

	<u>INDEX</u>	<u>SUBSEQUENT</u>	<u>ALL</u>	<u>%</u>
<u>RECURRENCE</u>	179	33	212	7
<u>DeNovo</u>	8	2	10	0.3

RETRANSPLANTATION

- **WHAT IS THE REPORTED INCIDENCE OF RECURRENCE OF THE PRIMARY RENAL DISEASE IN THE TRANSPLANTED KIDNEY?**
 - **COCHAT ET AL PEDIATR NEPHROL 24:2097, 2009**
 - **SPRANGERS & KUYPERS
TRANSPLANTATION REVIEWS 27:126, 2013**

RETRANSPLANTATION

<u>PRIMARY DISEASE</u>	<u>RECURRENCE RATE</u>	<u>GRAFT LOSS</u>
FSGS	14-50%	40-60%
aHUS	20-80%	10-83%
dHUS	0-1%	0-1%
MPGN TYPE I	30-70%	17-50%
MPGN TYPE II	66-100%	25-61%
SLE NEPHRITIS	0-30%	0-5%
IgA NEPHROPATHY	35-60%	7-10%
IgA VASCULITIS (HSP)	31-100%	8-22%

RETRANSPLANTATION

- **WHY IS THE INCIDENCE OF RECURRENCE SO VARIABLE?**

- **METHOD OF DIAGNOSIS?**

- **?PROTOCOL BIOPSY**
- **?CLINICALLY INDICATED BIOPSY**
- **?CLINICAL SYMPTOMS**
 - **HEMATURIA**
 - **PROTEINURIA**
 - **↓ eGFR**
 - **TMA**

RETRANSPLANTATION

- **WHAT BIOMARKERS CAN BE MONITORED EITHER PRIOR TO OR FOLLOWING RETRANSPLANTATION TO ASSESS THE POTENTIAL FOR SUBSEQUENT RECURRENCE IN A PATIENT WHO LOST A GRAFT DUE TO RECURRENCE OF THE ORIGINAL DISEASE IN THE NATIVE KIDNEY?**

RETRANSPLANTATION

RECURRENT DISEASE

FSGS

IgA NEPHROPATHY/HSP

aHUS

MPGN

SLE (APL SYNDROME)

ANTI-GBM DISEASE

MEMBRANOUS

BIOMARKER

?suPAR/SF

ANTI-GIgAI

**{ MAC/ALTERNATE
COMP PATHWAY }**

SLE SEROLOGY

ANTI-GBM ab

PLA2-R ab

RETRANSPLANTATION

- CAN THE INCIDENCE ($\pm 80\%$) OF RECURRENCE OF FSGS IN A PATIENT WHO LOST A GRAFT FROM RECURRENCE BE REDUCED?
- GONZALEZ ET AL (**PEDIATR TRANSPL 15:495, 2011**) NOTED RECURRENCE IN 2/5 PATIENTS WHO LOST AN INITIAL GRAFT FROM FSGS
RECURRENCE: 2/3 WHO DID NOT RECUR HAD >3 PRE-TRANSPLANT PLASMAPHERESIS,
WHEREAS, BOTH PATIENTS WHO RECURRED HAD <1 PLASMAPHERESIS

RETRANSPLANTATION

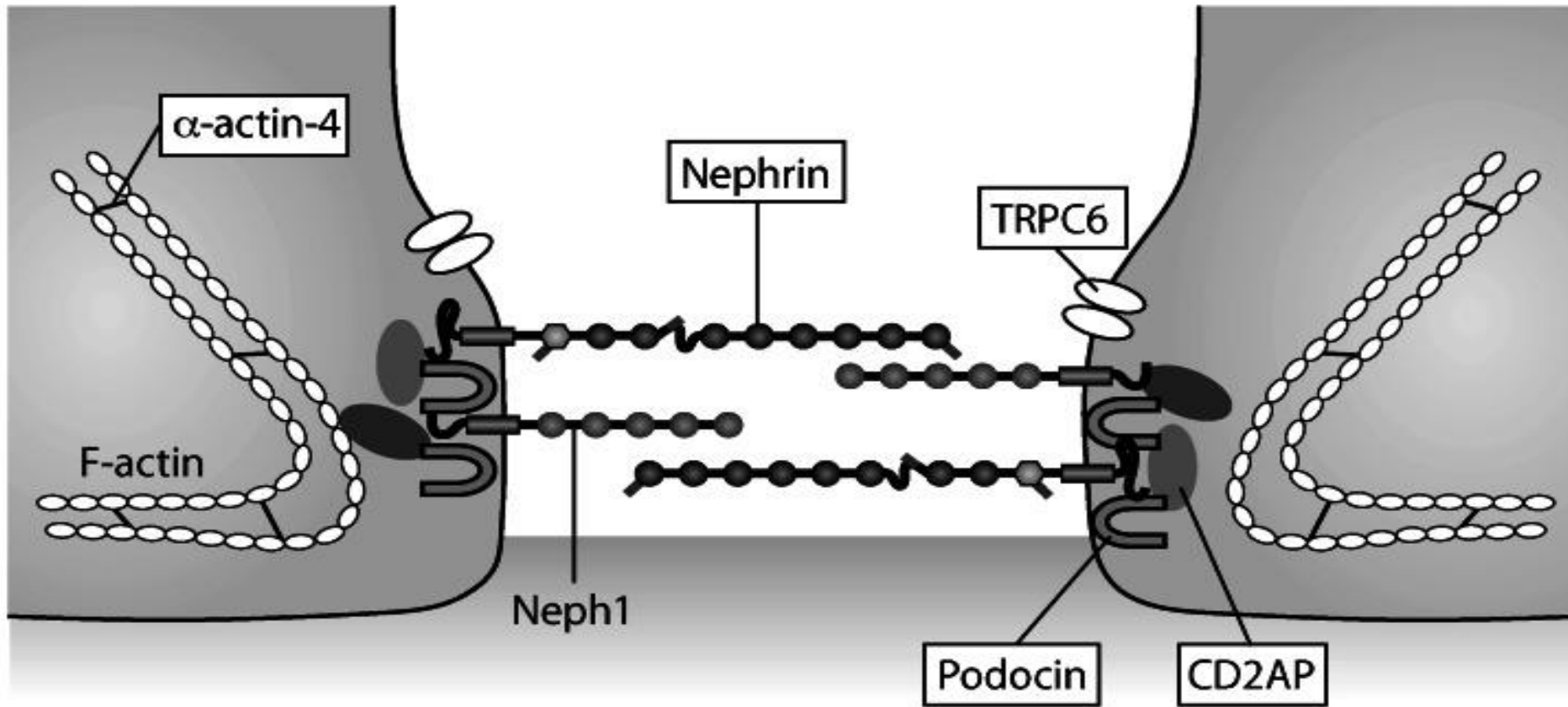
- **VASCULAR ENDOTHELIUM OF ANTIPHOSPHOLIPID NEPHROPATHY (APLN) IS ACTIVATED BY mTORC PATHWAY**
- **7/10 (70%) RECIPIENTS WITH APLN TREATED WITH SIROLIMUS HAD A FUNCTIONING GRAFT @ 144 MONTHS POST-TRANSPLANT COMPARED TO 3/27 (11%) NOT RECEIVING SIROLIMUS**
- **SIROLIMUS MAY PREVENT RECURRENCE OF APLN FOLLOWING INITIAL OR RETRANSPLANTATION**

RETRANSPLANTATION

- **REMOVAL OF ANTIBODIES TO NEOANTIGENS**
 - **ALPORT (ANTI-GBM ANTIBODIES)**
 - **CONGENITAL NEPHROTIC SYNDROME (NEPHRIN)**
 - **GENETIC FSGS (PODOCIN)**

RETRANSPLANTATION

Podocyte slit diaphragm



RETRANSPLANTATION

- **75% OF PRIMARY CONGENITAL NS CAUSED BY NPHS1 (NEPHRIN) AND NPHS2 (PODOCIN)**
- **63% OF NPHS1 CAUSED BY FIN-MAJOR/FIN-MAJOR MUTATIONS WITH A \pm 30% RATE OF RECURRENCE OF THE NEPHROTIC SYNDROME**
- **RECURRENCE CAUSED BY ANTI-NEPHRIN ANTIBODIES**
- **TREATMENT WITH METHYL-PREDNISOLONE, CYCLOPHOSPHAMIDE, PLASMAPHERESIS AND RITUXIMAB EFFECTIVE FOLLOWING INITIAL RECURRENCE AND RETRANSPLANTATION**

RETRANSPLANTATION

- **RECURRENCE OF THE NEPHROTIC SYNDROME IN HOMOZYGOUS OR COMPOUND HETEROZYGOUS NPHS2 MUTATIONS IS RARE (1-2%)**
- **NO ANTI-PODOCIN ANTI-BODIES REPORTED**
- **TREATMENT VARIABLE WITH PLASMAPHERESIS, METHYLPREDNISOLONE AND CYCLOPHOSPHAMIDE SUCCESSFUL**

RETRANSPLANTATION

- **WHAT SPECIFIC TREATMENTS MAY BE REQUIRED PRIOR TO RETRANSPLANTATION TO EITHER FACILITATE THE RETRANSPLANT OR REDUCE THE POTENTIAL FOR RECURRENCE?**

RETRANSPLANTATION

- **REDUCE ELIMINATE *PRA/DSA***
 - DESENSITIZATION PROTOCOL
 - DESENSITIZATION COMBINED WITH PAIRED DONOR EXCHANGE (**YABU ET AL TRANSPL PROC 45:82, 2013**)
- **REDUCE PUTATIVE BIOMARKER**
 - PLASMAPHERESIS/IVIgG/RITUXIMAB/BORTEZOMIB
- **CURTAIN COMPLEMENT ACTIVATION (aHUS, MPGN)**
 - ECULIZUMAB (**McCAUGHAN ET AL AJT 12:1046,201**)
 - LIVER-KIDNEY TRANSPLANT –aHUS (**TRAN ET AL PEDIAT NEPHROL 29:477, 2014**)

RETRANSPLANTATION

- **WHY IS IT IMPORTANT TO PERFORM GENETIC ANALYSIS ON BOTH DONOR AND RECIPIENT PRIOR TO RETRANSPLANTATION OF PATIENTS WITH STEC-HUS (dHUS)?**
 - **ALBERTI ET AL AJT 13:2201, 2013**

RETRANSPLANTATION

- **90% OF *dHUS* RECOVER AND <1% WHO ARE TRANSPLANTED RECUR**
- **RECURRENCE OCCURRED IN 2 PATIENTS WITH *dHUS***
- **GENETIC TESTING REVEALED**
 - ***CFI* HETEROZYGOUS MUTATION IN ONE RECIPIENT**
 - ***MCP* HETEROZYGOUS MUTATION IN BOTH DONOR (MOTHER) AND RECIPIENT IN THE OTHER**
- **GENETIC TESTING SHOULD BE PERFORMED PRIOR TO EVERY *LRD* Tx IN STEC-HUS ESRD**