

# **RETRANSPLANTATION FOLLOWING REJECTION AND RECURRENT DISEASE**

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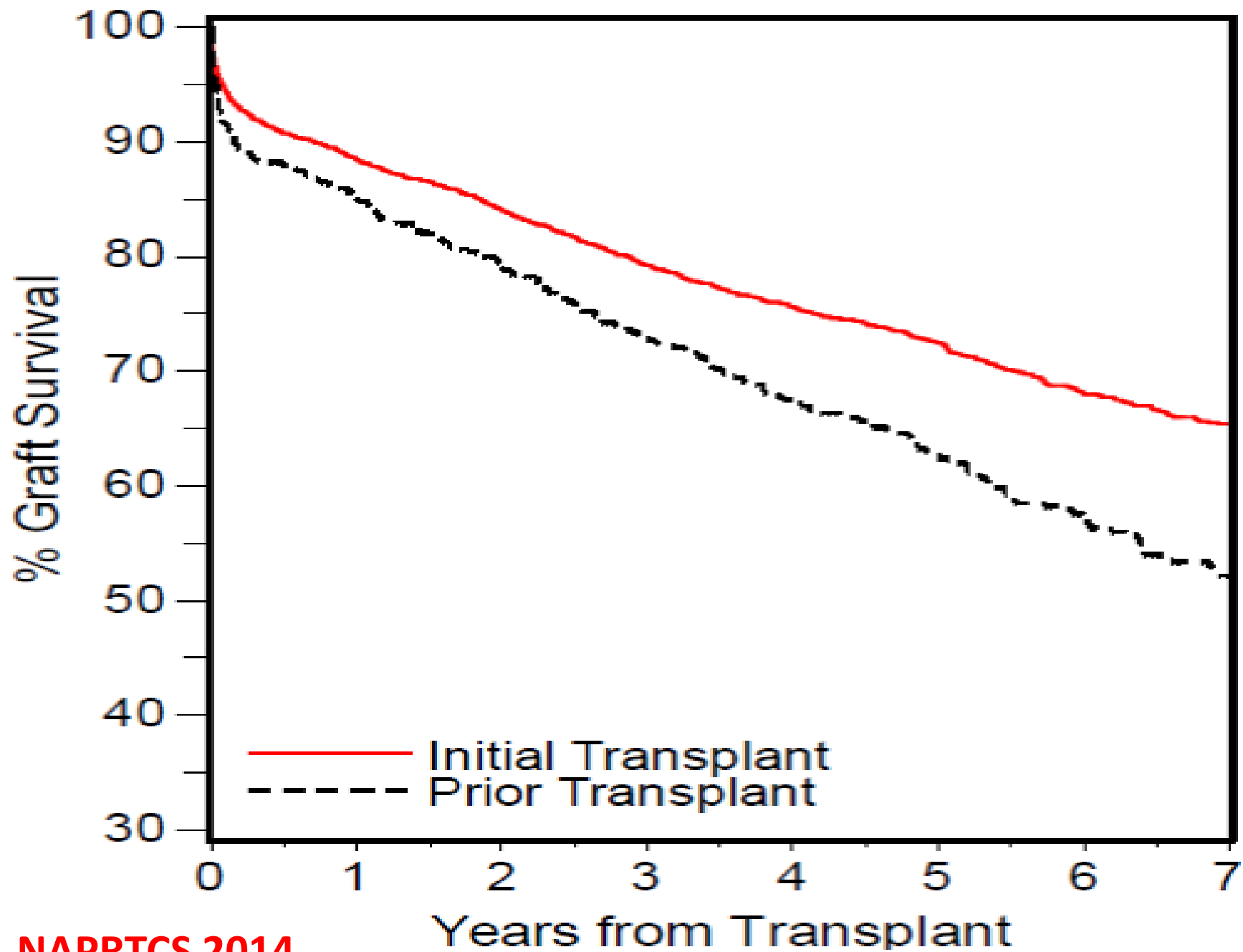
# RETRANSPLANTATION

- **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* 1<sup>ST</sup> AND 2<sup>ND</sup> GRAFTS HAD ↑ SURVIVAL RATE COMPARED TO 1<sup>ST</sup> AND 2<sup>ND</sup> *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 2<sup>ND</sup> GRAFT**
  - **↓ RATE OF 2<sup>ND</sup> TRANSPLANTATION ( ↓ BY 20%)**
  - **↓ REGRAFT SURVIVAL RATE**
    - **5 YR GRAFT SURVIVAL RATE ASSOCIATED WITH NUMBER OF 1<sup>ST</sup> AND 2<sup>ND</sup> 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 2<sup>nd</sup>**  
**TRANSPLANT AFTER A FAILED RENAL TRANSPLANT IN**  
**51 CHILDREN WHO SUFFERED GRAFT LOSS BETWEEN**  
**2003 -2011**

- **21/51(41%) RECEIVED A 2<sup>nd</sup> 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

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

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

# 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

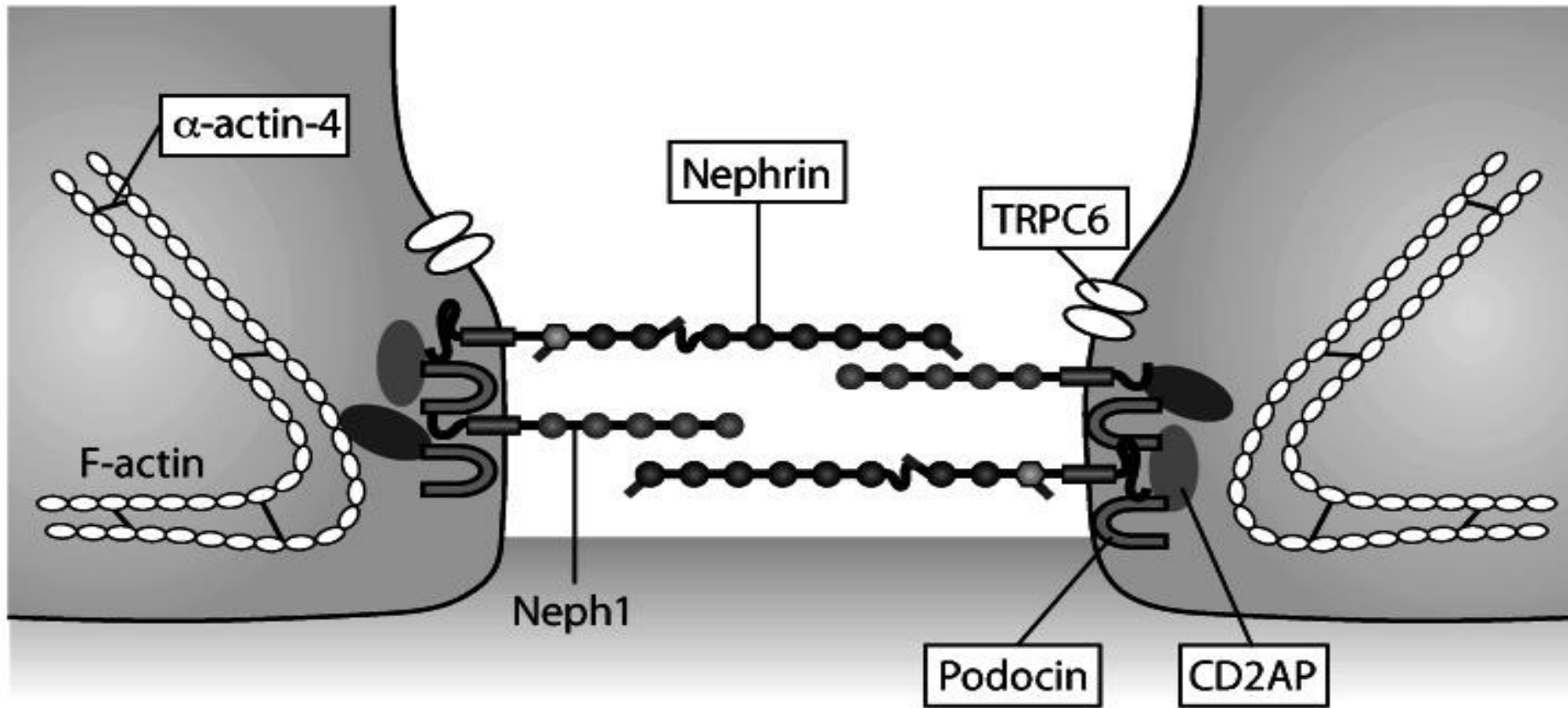
- **VASCULAR ENDOTHELIUM OF ANTIPHOSPHOLIPID NEPHROPATHY (APLN) IS ACTIVATED BY mTORC PATHWAY**
- **7/10 (70%) RECIPIENTS WITH APLN TREATED WITH SIROLIMUS HAD A FUNCTIONING GRAFT @ 144 MONTHS POST-TRANSPLANT COMPARED TO 3/27 (11%) NOT RECEIVING SIROLIMUS**
- **SIROLIMUS MAY PREVENT RECURRENCE OF APLN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