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
• WHAT IS THE CURRENT OUTCOME OF KIDNEY RETRANSPLANTATION COMPARED TO THAT OF THE INITIAL KIDNEY TRANSPLANT?
RETRANSPLANTATION: COMPARISION OF PRIMARY AND SUBSEQUENT GRAFT FAILURE RATES (NAPRTCS)

<table>
<thead>
<tr>
<th></th>
<th>LIVE RELATED DONOR (N=5819)</th>
<th>DECEASED DONOR (N=5298)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TOTAL FAILURE 5YR*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>NO PRIOR TRANSPLANT</td>
<td>88.7</td>
<td>19.1</td>
</tr>
<tr>
<td>PRIOR TRANSPLANT</td>
<td>11.3</td>
<td>28.1</td>
</tr>
<tr>
<td></td>
<td>NO PRIOR TRANSPLANT</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td>PRIOR TRANSPLANT</td>
<td>17</td>
</tr>
</tbody>
</table>

* 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%)
# RETRANSPANTATION

<table>
<thead>
<tr>
<th>GRAFT #</th>
<th>SURVIVAL RATE (YEARS)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>91.9%</td>
</tr>
<tr>
<td>2</td>
<td>89.3%</td>
</tr>
<tr>
<td>3</td>
<td>89.6%</td>
</tr>
<tr>
<td>4</td>
<td>84.9%</td>
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</tbody>
</table>

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 RETRANSPANTATION?
• ARE THERE MITIGATING TECHNICAL CIRCUMSTANCES IMPACTING RETRANSPANTATION?
• 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. ANTIENDOTHELIAL 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
• 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 AT TIME OF KIDNEY GRAFT FAILURE
  - MINORITY RACE
  - PUBLIC INSURANCE
  - ELEVATED PEAK %PRA (PANEL REACTIVE ANTIBODIES)
  - EARLIER INITIAL KIDNEY GRAFT FAILURE

VAN ARENDONK ET AL TRANSPLANTATION 96:487,2013
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 RETRANSPANTED 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 \textit{(Panel Reactive Antibodies)}/ DSA \textit{(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
RETROTRANSPLANTATION

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

  - 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

GRALLA ET AL TRANSPLANTATION 95:1218, 2013
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 RETRANSPPLANTED
  - 118/126 (93.7%) FUNCTIONING AS OF 6/09
  - 1 GRAFT LOST TO BKVN AND 17.5% RxED 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\textsuperscript{nd} TRANSPLANT AFTER A FAILED RENAL TRANSPLANT IN 51 CHILDREN WHO SUFFERED GRAFT LOSS BETWEEN 2003 - 2011
    • 21/51(41\%) RECEIVED A 2\textsuperscript{nd} 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

DUNN ET AL AM J TRANSPLANT 9:1337, 2009
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

DUNN ET AL AM J TRANSPLANT 9:1337, 2009
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)
# RETRANSPANTATION

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSGS</td>
<td>1308</td>
</tr>
<tr>
<td>CHRONIC GN</td>
<td>344</td>
</tr>
<tr>
<td>CONGENITAL NS</td>
<td>289</td>
</tr>
<tr>
<td>HUS</td>
<td>288</td>
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<tr>
<td>IDIOPATHIC RPGN</td>
<td>195</td>
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<tr>
<td>MPGN TYPE I</td>
<td>191</td>
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<tr>
<td>SYSTEMIC LE</td>
<td>172</td>
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<tr>
<td>IgA VASCULITIS (HSP)</td>
<td>115</td>
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<tr>
<td>MPGN TYPE II</td>
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<tr>
<td>WEGENER’S(POLYANGITIS/GRANULOMATOSIS)</td>
<td>71</td>
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<tr>
<td>MEMBRANEOUS GN</td>
<td>51</td>
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<tr>
<td>OTHER IMMUNOLGIC MEDIATED DISEASES</td>
<td>34</td>
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NAPRTCS 2014
RETRANSPLANTATION

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

<table>
<thead>
<tr>
<th>Recurrence</th>
<th>Index</th>
<th>Subsequent</th>
<th>All</th>
<th>%</th>
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<tbody>
<tr>
<td>Recurrence</td>
<td>179</td>
<td>33</td>
<td>212</td>
<td>7</td>
</tr>
<tr>
<td>DeNovo</td>
<td>8</td>
<td>2</td>
<td>10</td>
<td>0.3</td>
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</table>
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
<table>
<thead>
<tr>
<th>Primary Disease</th>
<th>Recurrence Rate</th>
<th>Graft Loss</th>
</tr>
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<tbody>
<tr>
<td>FSGS</td>
<td>14-50%</td>
<td>40-60%</td>
</tr>
<tr>
<td>aHUS</td>
<td>20-80%</td>
<td>10-83%</td>
</tr>
<tr>
<td>dHUS</td>
<td>0-1%</td>
<td>0-1%</td>
</tr>
<tr>
<td>MPGN Type I</td>
<td>30-70%</td>
<td>17-50%</td>
</tr>
<tr>
<td>MPGN Type II</td>
<td>66-100%</td>
<td>25-61%</td>
</tr>
<tr>
<td>SLE Nephritis</td>
<td>0-30%</td>
<td>0-5%</td>
</tr>
<tr>
<td>IgA Nephropathy</td>
<td>35-60%</td>
<td>7-10%</td>
</tr>
<tr>
<td>IgA Vasculitis (HSP)</td>
<td>31-100%</td>
<td>8-22%</td>
</tr>
</tbody>
</table>

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?
<table>
<thead>
<tr>
<th>RECURRENT DISEASE</th>
<th>BIOMARKER</th>
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<tbody>
<tr>
<td>FSGS</td>
<td>?suPAR/SF</td>
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<tr>
<td>IgA NEPHROPATHY/HSP</td>
<td>ANTI-GIgAI</td>
</tr>
<tr>
<td>aHUS</td>
<td>{ MAC/ALTERNATE</td>
</tr>
<tr>
<td>MPGN</td>
<td>COMP PATHWAY</td>
</tr>
<tr>
<td>SLE (APL SYNDROME)</td>
<td>SLE SEROLOGY</td>
</tr>
<tr>
<td>ANTI-GBM DISEASE</td>
<td>ANTI-GBM ab</td>
</tr>
<tr>
<td>MEMBRANOUS</td>
<td>PLA2-R ab</td>
</tr>
</tbody>
</table>
RETRANSPLANTATION

• CAN THE INCIDENCE (±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 PLASMAFHERESIS, WHEREAS, BOTH PATIENTS WHO RECURRED HAD <1 PLASMAFHERESIS
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

CANAUD ET AL NEJM 371:303, 2014
RETRANSPLANTATION

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

Podocyte slit diaphragm

α-actin-4

F-actin

Neph1

Nephrin

TRPC6

Podocin

CD2AP
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 ±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

HOLMBERG & JALANKO PEDIATR NEPHROL 29:2309, 2014
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

• CURTAIL COMPLEMENT ACTIVATION (aHUS, MPGN)
  – ECULIZUMAB (*McCAUGHAN ET AL AJT 12:1046, 201*1)
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