PRIMARY GLOMERULAR DISEASES

David Harris
8/2015
Steroid-sensitive & resistant nephrotic syndrome in children

Minimal-change disease and FSGS in children and adults

Idiopathic membranous nephropathy

Idiopathic membranoproliferative

GN associated with infections

IgA nephropathy & Henoch-Schönlein purpura

Lupus nephritis

Renal vasculitis

Antiglomerular basement membrane GN
MCD: Pathophysiology

T cell lymphokines

 Loss of anionic charge barrier & podocytes injury

 EM: foot process fusion
 no deposits

 LM & IF: minimal Δ

 Proteinuria
Kidney biopsy if (NG)

• late failure after initial response to corticosteroids
• a high index of suspicion for a different underlying pathology
• decreasing kidney function with CNIs

Vaccination (NG)

• pneumococcal
• influenza annually (& household contacts)
• defer live vaccines until prednisone dose < 1 mg/kg/d (<20 mg/d)
• no live vaccines if on immunosuppressives
• zoster immune globulin if close contact & on immunosuppressives
Minimal Lesion Disease in Adults

Prednisone as first-line therapy (1C)

Prednisone 1 mg/kg up to 80 mg daily or 2 mg/kg up to 120 (not 160) mg alternate days (2C) from 4 (minimum) to 16 weeks until remission (2C)

Taper over 6 months in remitters (2D)

For occasional relapses, treat as above until remission, and taper over at least 2 months (2D)
Cyclophosphamide 2-2.5 mg/kg for 8 weeks (2C)

OR

CNI for 1-2y for cyclophosphamide failures or those with fertility concerns (2C)

OR

MMF for 1-2y for those intolerant of all the drugs above (2D)

Note: no stated distinction between disease-treating agents like cyclophosphamide vs disease-modulating agents like cyclosporine
Earlier remission and lower incidence of relapse in patients with initial methylprednisolone use followed by prednisolone (mPSL+PSL group), compared with those with initial prednisolone use (PSL group).

Maki Shinzawa et al. CJASN 2014;9:1040-1048

Retrospective cohort, adults
Rituximab

Clinical response
– Yes: steroid-dependent or frequently relapsing nephrotic syndrome
– Limited: steroid-resistant, esp FSGS

No potentially life-threatening adverse events (so far)

Most reports retrospective and small case series

Kronbichler A & Bruchfeld A NCP 2014;128:277-82
Box plot of the number of NS relapses over 1 year of follow-up after rituximab administration, and during the year before rituximab administration in the study group as a whole (overall), and in different age (children versus adults) and diagnosis (MCD/MesG...
with first episode..

no ACEI in normotensive patients to decrease proteinuria (2D)

no statins for hyperlipidemia (2D)

continue to give steroids even if the patient is dialysis-dependent (rare) (2D)

(no comments about anti-coagulation or concomitant use of OCP)
Focal & segmental glomerulosclerosis

Clinical

• nephrotic or subacute proteinuria

• reduced GFR
• hypertension
• mild hematuria

• 10 - 50% ESRD @ 5 yrs
• Rx. ACEI

Renal biopsy
H & E

focal & segmental glomerular sclerosis
FSGS pathological variants

- perihilar FSGS
- glomerular tip lesion
- collapsing variant

Primary

Secondary

HIV, African
The rate of progression to ESRD for the three major subgroups is illustrated using Kaplan–Meier curves and the log-rank test.
Exclude secondary causes (NG)

Treat only if NS (1C)

**Prednisone** 1 mg/kg BW up to 80 mg daily, or 2 mg/kg BW up to 120 mg alternate days (2C)

Treat for a minimum of 4 weeks, and up to 16 weeks or until remission, whichever comes earlier (2D)

Taper prednisone over 6 months after remission achieved (2D)

**CNI** instead if cannot take/tolerate prednisone (2D)
FSGS: Secondary forms

Hereditary: Podocin, Nphrin, \( \alpha \)-Actinin-IV, TRP-c6, CDAP, Wt-1, COLIVa5, etc (n=30). AD, AR, X-linked, mitochondrial inheritance

Infectious: HIV, parvovirus B-19, polyomavirus (?)

Neoplasia: Carcinomas, lymphomas

Drugs: Bisphosphonates, heroin, interferon (\( \alpha, \beta, \gamma \)), CsA, Tac, ? NSAIDS

Mediated by adaptive structural-functional responses:

- Oligonephronia: agenesis, dysplasia, VUR, chronic allograft nephropathy
- Maladaptive (Normal renal mass): vaso-occlusive processes, obesity, sickle cell anemia, cyanotic CHD

Other: Any other primary/secondary glomerular disease (IgAN, MN, LN, vasculitis, DN)

D'Agati et al, 2004
# PRIMARY vs SECONDARY

<table>
<thead>
<tr>
<th></th>
<th>PRIMARY</th>
<th>SECONDARY</th>
</tr>
</thead>
<tbody>
<tr>
<td>onset</td>
<td>abrupt</td>
<td>insidious</td>
</tr>
<tr>
<td>hypoalbuminaemia/oedema</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>fp effacement</td>
<td>extensive</td>
<td>mild</td>
</tr>
<tr>
<td>antiproteinuria with ACEi</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>other</td>
<td></td>
<td>obesity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hilar variant</td>
</tr>
<tr>
<td></td>
<td></td>
<td>glomerulomegaly</td>
</tr>
</tbody>
</table>
FSGS: Relapses and Steroid-Resistance

Relapses

treat as for minimal lesion relapses (2D)

Steroid resistant

cyclosporine 3-5 mg/kg BW for at least 4-6 months (2B)

if complete response or partial response: continue cyclosporine for at least 12 months, followed by gradual taper (2D)

MMF & high dose dexamethasone if intolerant of cyclosporine (2C)

(Opinion: longer term lower dose cyclosporine can be effective)
Clinical context as therapeutic contra-indication

Immunosuppression (vs none)
  secondary

Prednisone (vs CyA)
  (pre)diabetes, obesity

Tacrolimus (vs CyA)
  (pre)diabetes
Membranous GN

• commonest cause of adult nephrotic syndrome
• idiopathic or 2°

Thickened GBM

• subepithelial deposits
• “spikes”
• “tram tracks”
IDIOPATHIC MEMBRANOUS NEPHROPATHY

Exclude secondary causes (Not Graded)

- autoimmune
- cancer
- infections
- drugs/toxins
- miscellaneous

Hints:

✔ absence of IgG4 against M-type phospholipase A2 receptor
✔ IgG1, IgG2, IgG3
✔ children
✔ young female: SLE
✔ E Asia: HBV
✔ >65y: cancer
✔ drugs: NSAIDs
IDIOPATHIC MEMBRANOUS NEPHROPATHY

IMMUNOSUPPRESSIVES:

YES  
Nephrotic syndrome  +  
proteinuria > 4 g/d + >50% of baseline, + no decline with antihypertensives for > 6m \((1B)\) &/or 
severe, disabling nephrosis \((1C)\) &/or 
unexplained SCR rise > 30% in 6-12m \((2C)\)

NO  
SCR 300 μmol/l  +  
small kidney or 
severe infections \((Not Graded)\)
IDIOPATHIC MEMBRANOUS NEPHROPATHY

INITIAL THERAPY

6m monthly steroids (PO or IV) alternating with monthly cyclophosphamide (PO)* (1B)

cyclophosphamide not chlorambucil (2B)

failure = no remission after 6m or rising Scr or severe nephrosis (1C)

repeat biopsy: rapid rise Scr + proteinuria <15 g/d (Not Graded)

cyclophosphamide: adjust dose for age & eGFR (Not Graded)

continuous oral cyclophosphamide: effective but more toxicity (2C)

*Ponticelli regimen: methylprednisolone (1g/d IV X3 → 0.5mg/kg/d) then cyclophosphamide (2mg/kg/d)
IDIOPATHIC MEMBRANOUS NEPHROPATHY

Spontaneous remission: 20% complete, 20% partial; after up to 2y

Persistent nephrosis in 50%

of these 30-40% → ESKD in 10y

high risk if >8g/d

Troyanov S et al. KI 2004;66:1199-1205
Withdrawal (herpes zoster)
cyclophosphamide 2 (0)
chlorambucil 6 (4)

Who uses Ponticelli??

Ponticelli C et al.
Kid Int 1995:48:1600-4

Ponticelli et al.
JASN 1998;9:444-50
IDIOPATHIC MEMBRANOUS NEPHROPATHY

ALTERNATIVE INITIAL THERAPY

CNI >6 months (1C)*

stop if no remission in 6m (2C)

reduce dose every 1-2m to 50% & continue (2C)

monitor CNI blood levels (Not Graded)

*cyclosporin 1.75-2.5 mg/kg bid + prednisolone 0.15mg/kg/d

tacrolimus 0.025-0.0375 mg/kg bid + no prednisolone

(CNI toxicity less likely than with solid organ transplant because of lower doses)

?? ACTH, rituximab
Cattran et al.  
*Kidney Int* 2001;59:1484-1490

Steroid-resistant.  
cyclosporin vs placebo for 26w  
40% relapse in both

Praga M et al.  
*Kidney Int* 2007;71:924-930

tacrolimus vs nil for 52w  
~50% relapse
IDIOPATHIC MEMBRANOUS NEPHROPATHY

DO NOT USE:

corticosteroids alone (1B)

MMF alone (2C)

Chan TM et al. Nephrology 2007;12:576-81

MMF + pred vs Ponticelli
IDIOPATHIC MEMBRANOUS NEPHROPATHY

RESISTANT TO INITIAL THERAPY (10-30%)

- use alternative initial therapy (2C)

RELAPSE

- use same initial therapy (2D)
- but, repeat 6m cyclical steroid/cyclophosphamide only once (2B)
IDIOPATHIC MEMBRANOUS NEPHROPATHY

CHILDREN

as for adults (2C)

but, do not repeat cyclical steroid/cyclophosphamide (2D)

PROPHYLACTIC ANTICOAGULANTS

if serum albumin <25 g/l + additional prothrombotic risks*

oral warfarin (2C)

*> 10g/day proteinuria
BMI > 35
previous thromboembolism
family history or genetic predisposition to thromboembolism
prolonged immobilization or recent abdo or orthopaedic surgery
NYHA Class III or IV CHF
Table 2. Possible treatment choices in patients with idiopathic (primary) membranous nephropathy

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Results</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroids alone</td>
<td>No benefit</td>
<td>Although ineffective, frequently used by practitioner</td>
</tr>
<tr>
<td>Steroids-alkylating agents</td>
<td>Can significantly increase the probability of complete or partial remission. Protect renal function in the long term</td>
<td>The results are confirmed by randomized controlled trials. Risk of side effects (infection, leucopenia). Avoid frequent repetitions (risk of oncogenic or gonadotoxic effects)</td>
</tr>
<tr>
<td>CNI</td>
<td>Can significantly reduce the amount of proteinuria and increase the probability of complete or partial remission. Little information about their effects on renal function</td>
<td>Relapse of proteinuria is frequent after CNI withdrawal. Risk of hypertension, nephrotoxicity. Little information about long-term safety</td>
</tr>
<tr>
<td>Mycophenolate salts</td>
<td>Ineffective when given alone. Can reduce proteinuria when given together with steroids</td>
<td>Only small-sized studies with short-term follow-up are available. High relapse rate. No information about the long-term safety and efficacy</td>
</tr>
<tr>
<td>ACTH</td>
<td>Can reduce proteinuria</td>
<td>Only few small-sized studies with short-term follow-up are available. A randomized controlled trial is in progress</td>
</tr>
<tr>
<td>Rituximab</td>
<td>Can reduce proteinuria</td>
<td>Large observational studies available. No head-to-head comparison with other treatments</td>
</tr>
</tbody>
</table>

CNI, calcineurin inhibitors; ACTH, adrenocorticotropic hormone.
IDIOPATHIC MEMBRANOPROLIFERATIVE GN

EVALUATION

look for underlying diseases (Not Graded)

chronic infection (esp HCV)
autoimmune (esp SLE)
monoclonal gammopathy (esp LCDD & mc IgG disease)
complement dysregulation (esp factor H)
chronic & healed thrombotic microangiopathy

TREATMENT

oral cyclophosphamide or MMF + low-dose alternate-day or daily corticosteroids for < 6m if nephrosis + progressive rise in Scr (2D)
C3 Glomerulopathy

Morphological appearance

- Glomerulonephritis with dominant C3

Disease category

- C3 glomerulopathy
- Post-infectious GN
- Other

C3 glomerulopathy

- DDD
  - Specific genetic forms and/or autoantibodies
  - Not otherwise specified

- C3 GN
  - Specific genetic forms for example CFHR5 nephropathy and/or autoantibodies
  - Not otherwise specified

Pickering MC et al. KI 2013;84:1079-89
## Complement investigations in C3 glomerulopathy

### Tests recommended in all patients

<table>
<thead>
<tr>
<th>Test</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measurement of serum C3 and C4</td>
<td>Low C3 with normal C4 indicates alternative pathway activation</td>
</tr>
<tr>
<td>Measurement of C3 nephritic factor</td>
<td>C3 nephritic factors are associated with C3 glomerulopathy; their correlation with disease course is unclear</td>
</tr>
<tr>
<td>Measurement of serum factor H</td>
<td>Factor H deficiency is associated with C3 glomerulopathy and is invariably associated with reduction in serum C3 activation</td>
</tr>
<tr>
<td>Serum paraprotein detection</td>
<td>Paraproteinemia associated with C3 glomerulopathy, specialist tests required to determine whether paraprotein is a cause of uncontrolled C3 activation</td>
</tr>
<tr>
<td>Screening for CFHR5 mutation</td>
<td>CFHR5 nephropathy is a well-characterized cause of C3 glomerulopathy and thus screening for this mutation is clinically informative</td>
</tr>
</tbody>
</table>

### Tests that should be considered on a case-by-case basis as they require expert interpretation and/or clinical validation

- Measurement of serum factor B
- Measurement of serum C5
- Measurement of markers of C3 activation, e.g., C3d, C3c, C3adesArg
- Measurement of markers of C5 activation, e.g., C5adesArg, soluble C5b-9
- Measurement of anti-factor H autoantibodies
- Anti-factor B autoantibodies
- Mutation screening of complement regulatory genes (e.g., CFH, CFI, CD46), activation protein genes (C3, CFB) and assessment of copy number variation across the CFH-CFHR locus

### Comment
- Uncontrolled alternative pathway activation may be associated with reduced factor B levels
- May be reduced in terminal pathway activation and could indicate group most likely to benefit from therapeutic C5 inhibition
- Activated C3 components are more sensitive markers of C3 activation than antigenic levels of intact C3
- Activated C5 components are more sensitive markers of C5 activation than antigenic levels of intact C5
- Anti-factor H autoantibodies are associated with C3 glomerulopathy; correlation with disease course is unclear; especially important to measure in patients with low C3 and negative C3 nephritic factor
- Anti-factor B autoantibodies are associated with C3 glomerulopathy; correlation with disease course is unclear
- Mutations in these genes associated with C3 glomerulopathy; especially important to screen for CFH mutations in patients with low C3 and negative C3 nephritic factor

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Pickering MC et al. KI 2013;84:1079-89
Pathogenesis of IgA nephropathy

Hit #1: Increased Gal-deficient IgA1

Hit #2: Production of unique anti-glycan antibodies

Hit #3: Formation of pathogenic IgA1-containing circulating immune complexes

Hit #4: Glomerular injury

- Proliferation
- ECM production
- Cytokines
- Growth factors

Mesangial cell

Podocyte

IgA1 complexes
IgA nephropathy

Mesangium:
LM: Cellular proliferation & matrix
EM: Electron dense deposits
IF: IgA
REMISSION OF PROTEINURIA IMPROVES PROGNOSIS IN IgA NEPHROPATHY

Reich H et al. JASN 2007; 18: 3177

**Time-average proteinuria**
- 1 - < 1g/24h
- 2 – 1-2 g/24h
- 3 – 2-3g/24h
- 4 - >3g/24h
IgA NEPHROPATHY

INITIAL EVALUATION (NG)

Assess

for secondary causes of IgAN

risk of progression: proteinuria, BP & eGFR at diagnosis & follow-up

+/- pathological features for prognosis
<table>
<thead>
<tr>
<th>Feature</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesangial hypercellularity</td>
<td>M0 or M1</td>
</tr>
<tr>
<td>Endocapillary hypercellularity</td>
<td>E0 or E1</td>
</tr>
<tr>
<td>Segmental sclerosis/adhesions</td>
<td>S0 or S1</td>
</tr>
<tr>
<td>Tubular atrophy/interstitial fibrosis</td>
<td>T0 or T1 or T2</td>
</tr>
</tbody>
</table>

...validation studies are required
IgA NEPHROPATHY

ANTIPROTEINURIC & ANTIHYPERTENSIVE THERAPY

long-term ACE-I or ARB

for proteinuria >1 g/d, with uptitration depending on BP (1B)

for proteinuria 0.5 to 1 g/d (in children, 0.5 to 1 g/d/1.73 m²) (2D)

uptitration as far as tolerated to achieve proteinuria <1 g/d. (2C)

BP goal (NG)

<130/80 mmHg with proteinuria <1 g/d

<125/75 mmHg when initial proteinuria is >1 g/d
IgA NEPHROPATHY

CORTICOSTEROIDS

for 6m if persistent proteinuria $\geq$1 g/d, despite 3-6m of optimized supportive care (ACE-I or ARBs, BP control) & GFR $>50$ ml/min (2C)
Effect of steroids on proteinuria in patients with IgA nephropathy.

<table>
<thead>
<tr>
<th>Study</th>
<th>Steroid Mean</th>
<th>Steroid SD</th>
<th>Steroid Total</th>
<th>Control Mean</th>
<th>Control SD</th>
<th>Control Total</th>
<th>Mean Difference</th>
<th>Mean Difference 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lai 1986</td>
<td>2.3</td>
<td>2.2</td>
<td>17</td>
<td>3.3</td>
<td>2.1</td>
<td>17</td>
<td>-1.00</td>
<td>[-2.45, 0.45]</td>
</tr>
<tr>
<td>Julian 1993</td>
<td>1.3</td>
<td>0.3</td>
<td>17</td>
<td>1.8</td>
<td>0.7</td>
<td>18</td>
<td>-0.50</td>
<td>[-0.85, -0.15]</td>
</tr>
<tr>
<td>Shoji 2000</td>
<td>0.29</td>
<td>0.23</td>
<td>11</td>
<td>0.71</td>
<td>0.39</td>
<td>8</td>
<td>-0.42</td>
<td>[-0.73, -0.12]</td>
</tr>
<tr>
<td>Koike M 2008</td>
<td>0.31</td>
<td>0.51</td>
<td>24</td>
<td>0.68</td>
<td>0.69</td>
<td>24</td>
<td>-0.37</td>
<td>[-0.71, -0.03]</td>
</tr>
<tr>
<td>Lv 2009</td>
<td>1.04</td>
<td>0.54</td>
<td>33</td>
<td>1.57</td>
<td>0.86</td>
<td>30</td>
<td>-0.53</td>
<td>[-0.89, -0.17]</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td>102</td>
<td></td>
<td></td>
<td>97</td>
<td>-0.46</td>
<td>[-0.63, -0.29]</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 1.05, df = 4 (P = 0.90); I² = 0%
Test for overall effect: Z = 5.36 (P < 0.00001)

Exclude Lai 1986 (95% CI) 85 80
Heterogeneity: Chi² = 0.51, df = 3 (P = 0.92); I² = 0%
Test for overall effect: Z = 5.24 (P < 0.00001)

Jicheng Lv et al. JASN 2012;23:1108-1116

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Effect of steroids on composite renal endpoint (ESRD or doubling of serum creatinine or halving of GFR) in patients with IgA nephropathy.

<table>
<thead>
<tr>
<th>Study</th>
<th>Steroids group event/total</th>
<th>Control group event/total</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Julian 1993</td>
<td>1/17</td>
<td>2/18</td>
<td>0.53 (0.05, 5.32)</td>
</tr>
<tr>
<td>Katafuchi 2003</td>
<td>3/43</td>
<td>3/47</td>
<td>1.09 (0.23, 5.13)</td>
</tr>
<tr>
<td>Lai 1986</td>
<td>0/17</td>
<td>0/17</td>
<td>1.00 (0.00, 90105.34)</td>
</tr>
<tr>
<td>Lv 2009</td>
<td>0/33</td>
<td>2/30</td>
<td>0.18 (0.01, 3.64)</td>
</tr>
<tr>
<td>Manno 2009</td>
<td>2/48</td>
<td>13/49</td>
<td>0.16 (0.04, 0.66)</td>
</tr>
<tr>
<td>Pozzi 2004</td>
<td>1/43</td>
<td>13/43</td>
<td>0.08 (0.01, 0.56)</td>
</tr>
<tr>
<td>Shoji 2000</td>
<td>0/11</td>
<td>0/8</td>
<td>0.73 (0.00, 6856.08)</td>
</tr>
<tr>
<td>Hogg 2006</td>
<td>2/33</td>
<td>4/31</td>
<td>0.47 (0.09, 2.39)</td>
</tr>
<tr>
<td>Overall</td>
<td>9/245</td>
<td>37/243</td>
<td>0.32 (0.15, 0.67) p=0.002</td>
</tr>
</tbody>
</table>

$I^2 = 0.0 \%$, $p = 0.545$

Weights are from random effects analysis

Proteinuria >1g/d, normal renal function

Jicheng Lv et al. JASN 2012;23:1108-1116
IgA NEPHROPATHY

IMMUNOSUPPRESSIVE AGENTS

*not* cyclophosphamide or azathioprine

with corticosteroids, unless RPGN (2D)

with GFR <30 ml/min, unless RPGN (2C)

*not* MMF in IgAN (2C)
CONTROLLED PROSPECTIVE TRIAL OF STEROIDS AND CYTOTOXICS IN PROGRESSIVE IgA NEPHROPATHY

% Renal survival

Mean achieved BP 145/85

? ACEi

Ballardie, Roberts JASN 2002; 13: 142
## MYCOPHENOLATE IN IgA NEPHROPATHY

<table>
<thead>
<tr>
<th>Country</th>
<th>Study Year</th>
<th>Benefit</th>
<th>BP Achieved</th>
<th>ACE Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>BELGIUM</td>
<td>Maes 2004</td>
<td>None</td>
<td>125/73</td>
<td>100% salt restricted</td>
</tr>
<tr>
<td>HONG KONG</td>
<td>Tang 2005</td>
<td>Proteinuria reduced</td>
<td>122/71</td>
<td>100%</td>
</tr>
</tbody>
</table>
**LONG TERM BENEFITS OF 6 MONTHS MYCOPHENOLATE IN IgA NEPHROPATHY**

![Table showing results of Mycophenolate therapy vs control.](image)

<table>
<thead>
<tr>
<th></th>
<th>Mycophenolate</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteinuria</td>
<td>Reduced</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 months only</td>
<td></td>
</tr>
<tr>
<td>Slope eGFR</td>
<td>Less</td>
<td></td>
</tr>
<tr>
<td>Composite end point</td>
<td>3/20</td>
<td>10/20</td>
</tr>
<tr>
<td><em>Double sCr or ESRD</em></td>
<td></td>
<td><em>Significant difference</em></td>
</tr>
</tbody>
</table>

*Tang S et al. KI 2010; 77: 543*
IgA NEPHROPATHY

OTHER TREATMENTS

Fish oil
  persistent proteinuria ≥1 g/d, despite 3-6m supportive care (2D)

Tonsillectomy
  no (2D)
FISH OIL TREATMENT FOR IgA NEPHROPATHY

Randomised controlled trial – serum creatinine 130-265 mol/L

Donadio JASN 1999; 10: 1772

no benefit in 4 other small trials
Atypical IgAN

MCD with mesangial IgA deposits
  treat as for MCD if nephrotic (2B)

AKI + macroscopic hematuria
  repeat kidney biopsy if no improvement in 5d (NG)
  supportive care if only ATN & intratubular RCC (2C)

Crescentic IgAN (>50% crescents + RPGN) (NG)
  steroids & cyclophosphamide (2D)
Corticosteroids: complete remission of nephrotic syndrome

Microscopic haematuria persists

coincidence of MCD & IgAN
## CRESCENTIC GLOMERULONEPHRITIS

### Renal outcome with best known treatment

<table>
<thead>
<tr>
<th>Condition</th>
<th>1 year</th>
<th>5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic vasculitis</td>
<td>80%</td>
<td>75%</td>
</tr>
<tr>
<td>Goodpasture’s</td>
<td>70%</td>
<td>50%</td>
</tr>
<tr>
<td>Crescentic IgA nephropathy*</td>
<td>50%</td>
<td>20%</td>
</tr>
</tbody>
</table>

*small trials; variable selection criteria*