Primary or Secondary?

Drs. Siu Ngai Lau, A Tang
Renal unit
Department of Medicine & Geriatrics
United Christian Hospital
History

- Madam MH Chan, F/36, working as a nurse before

- NSND

- PMH:
  - Hepatitis B carrier with liver biopsy done in PWH in 1996
  - Liver biopsy diagnosis: chronic hepatitis, mild activity (mild chronic active hepatitis), HBV related
  - Fu private with blood tests and USG abdomen
• December, 2006

• She presented to AED with
  – Acute generalised edema x 3/7
  – Significant weight gain (18 lb in 1 week)
  – No skin rash
  – No joint pain
  – No systemic symptoms
Physical Examination

- Urine: albumin 4+, RBC moderate, WBC –
- Afebrile, No P/J, JVP not elevated
- BP 105 / 74 mHg, pulse 80 bpm
- No stigmata of chronic liver disease
- Facial puffiness, ankle edema 2+
- No lymphoadenopathy
- Chest, CVS: unremarkable
- Abdomen: Ascite +, no organomegaly
## Baseline Investigations

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
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<tbody>
<tr>
<td>WBC</td>
<td>4.7 x10^9/L</td>
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<tr>
<td>Hb</td>
<td>13.0 g/dL</td>
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<tr>
<td>platelet</td>
<td>217 x10^9/L</td>
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<tr>
<td>Urea</td>
<td>6.0 mmol/L</td>
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<tr>
<td>Creatinine</td>
<td>57 umol/L</td>
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<tr>
<td>Na</td>
<td>141 mmol/L</td>
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<tr>
<td>K</td>
<td>4.0 mmol/L</td>
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<tr>
<td>Serum Alb</td>
<td>18 g/L</td>
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<tr>
<td>Bilirubin</td>
<td>2 umol/L</td>
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<tr>
<td>ALP</td>
<td>68 IU/L</td>
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<tr>
<td>ALT</td>
<td>29 IU/L</td>
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<tr>
<td>Ca</td>
<td>1.92 mmol/L</td>
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<tr>
<td>PO4</td>
<td>1.36 mmol/L</td>
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<tr>
<td>Urate</td>
<td>0.285 mmol/L</td>
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</table>
## Baseline Investigations

<table>
<thead>
<tr>
<th>Test</th>
<th>Result (mmol/L)</th>
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<tbody>
<tr>
<td>Total cholesterol</td>
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<tr>
<td>LDL-cholesterol</td>
<td>5.31</td>
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<tr>
<td>HDL-cholesterol</td>
<td>3.55</td>
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<tr>
<td>Triglyceride</td>
<td>1.1</td>
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<tr>
<td>FBS</td>
<td>5.7</td>
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</table>
Baseline Investigations

- 24hr urine protein 6.69 g/day
- CrCl 122 mL/min
- MSU : mod RBC, no dysmorphic RBC
- USG abdomen :
  - Both kidney size 10cm with normal cortical echogenicity
  - The echogenicity of liver is within normal limit. No focal hepatic lesion.
  - Marked ascites
Further History

- Denied taking any herbs / O-T-C drugs
- No FHx of kidney disease/ neoplasm
Further Investigations

- HBsAg: +ve, HBeAg: +ve, Anti-HBe: -ve
- HBV DNA: > 10^6 copies/ml
- Anti-HCV: -ve
- Streptozyme: < 100 units
- VDRL: Non-reactive
- Anti-HIV: -ve
Further Investigations

- ANA: -ve
- Rheumatoid Factor: -ve
- C3/C4: normal
- CRP: normal
- ESR: 61 mm/hr
- Serum and urine protein electrophoresis: no paraprotein
Summary

A hepatitis B carrier lady presented with full blown nephrotic syndrome
Any Questions?
DDx of Nephrotic syndrome

- Glomerulonephritis secondary to Infection
  - hepatitis B
- Primary Glomerulonephritis
- Drugs
  - gold, penicillamine, captopril, NSAID, mercury, chinese herbs
- Connective tissue disease
  - SLE
- Diabetes mellitus
- Myeloma
- Amyloidosis
Next Step ?
IgA nephropathy?

- IF:
  - mild segmental mesangial and paramesangial deposition of IgA (+), and IgM (++)

- EM:
  - Definite evidence of membranous GN is not seen.

- Immunostains for HBsAg and HBeAg are negative.
IgAN + Hepatitis B
Vs
HBV-associated nephropathy
• Suggest to treat as nephrotic IgAN with high dose steroid

• 86 patients
• 6-month course of steroid treatment
• Either supportive therapy or steroid treatment (IV methylprednisolone)
• 9/43 patients in steroid group and 14/43 in control group reached endpoint (50% increase in plasma creatinine) by 5 year

Pozzi C et al. Lancet 1999
Our Treatment

- Started Lamivudine Dec., 2006
- Changed to Entecavir (SFI) Jan., 2007

- Rx: Zocor / Telmisartan

- 6 months later:
  - Nephrotic syndrome in remission
  - Seroconversion of HBeAg
Progress (~ 1y later)

- Dx: Hepatitis B virus associated nephropathy
- Plan for life long entecavir
- Patient self stopped Entecavir as desired for baby
Progress (~ 2 y later)

- Nephrotic syndrome in remission
- Albumin 49 g/L
- Proteinuria < 0.06g/d
- HBV DNA 1.4x10^4 cp/ml
- HBeAg –ve, anti- HBe +ve
HBV DNA (cp/ml)

* Lamivudine * Entecavir

**Seroconversion of HBeAg**

**Months from presentation**

**Serum albumin level (g/L)**

**Amount of proteinuria (g/d)**

- Serum albumin
- Proteinuria
Summary

Young lady with HBV-associated nephropathy, treated with entecavir
Hepatitis B Virus-Associated Nephropathy
• ~ 350 – 400 million people worldwide are infected with HBV

• The reported prevalence of HBV-associated nephropathy closely parallels to geographic patterns of prevalence of HBV
Extrahepatic manifestation

- Prevalence: relatively low, but it can be associated with significant morbidity and even mortality.

- Serum-sickness like "arthritis-dermatitis" prodrome
  - is seen in approximately one third of patients acquiring HBV
  - consisting of skin eruptions, urticaria and polyarthralgias or arthritis

- Skin rash
- Arthritis
- Arthralgia
- Glomerulonephritis
- Palpable purpura, papular acrodermatitis
- Typical polyarteritis nodosa
  - have persistent hepatitis B surface antigenemia (HBs Ag).

Pyrsopoulos NT et al., Curr Gastroenterol Rep. 2001
Han SH. Clin Liver Dis. 2004
Renal manifestation of hepatitis B virus

Membranous nephropathy
Membranoproliferative glomerulonephritis
Mesangial proliferative glomerulonephritis
IgA nephropathy
Serum-sickness-like syndrome
Polyarteritis nodosa
Lupus nephritis¹
Crescentic glomerulonephritis¹
Focal segmental glomerulosclerosis¹
Minimal change nephrotic syndrome¹

¹ Most likely incidental findings.

Rajendra Bhimma et al. Am J of Nephrology 2004
Mechanisms of virus-induced kidney injury

- Glomerulonephritis (GN)
  - Cytopathic effect of virus
  - Insitu immune complex formation
  - Circulating immune complexes

- Tubulointerstitial nephritis
  - Direct cytopathic effect
  - Mediated through host inflammatory response and/or viral protein

Hypothesis for the pathogenetic mechanism in the development of hepatitis B virus-associated membranous nephropathy

### HBV-associated nephropathy differences in clinical presentation between children & adults

<table>
<thead>
<tr>
<th></th>
<th>Children</th>
<th>Adults</th>
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<tbody>
<tr>
<td><strong>Mode of transmission</strong></td>
<td>Vertical transmission in the Far East</td>
<td>Often unknown</td>
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<td>Horizontal transmission in USA, Africa and Europe</td>
<td>Horizontal transmission in areas of high endemicity;</td>
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<td>in areas of low endemicity often associated with drug abuse or sexual</td>
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<td></td>
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<td>transmission</td>
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<td><strong>Clinical presentation</strong></td>
<td>Asymptomatic – detected by routine urine and serological</td>
<td>Nephrotic syndrome and proteinuria</td>
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<td>screening</td>
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<td>Nephrotic syndrome</td>
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<tr>
<td><strong>Gender</strong></td>
<td>Strong male dominance (&gt;80%)</td>
<td>Less pronounced male dominance</td>
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<td><strong>Mean age of presentation</strong></td>
<td>Horizontal transmission: 5–7 years</td>
<td>Any age group</td>
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<td>Vertical transmission: Infancy</td>
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<td><strong>Acute hepatitis</strong></td>
<td>Low incidence</td>
<td>Often present in adults from non-endemic areas where HBV MN associated</td>
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<td>with intravenous drug abuse, homosexuality and acquired immune</td>
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<td><strong>Histology</strong></td>
<td>Membranous (&gt;85%)</td>
<td>Usually membranous</td>
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<td>Often associated with IgA nephropathy</td>
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<td><strong>Renal function</strong></td>
<td>Preservation of renal function in over 95% of children</td>
<td>Progression to renal failure in 25%</td>
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</table>

Membranous Nephropathy

- Secondary MN was more common than idiopathic in Chinese.

- MN, and most secondary MN diagnoses were secondary to systemic lupus erythematosus and hepatitis B infection.

History of HBV associated nephropathy

• 1974: An immune complex type of glomerulonephritis may occur following hepatitis B virus infection, usually in association with chronic active hepatitis.

  Brzosko WJ et al. Lancet 1974

• 1979: Etiology of membranous nephropathy in children: Association between membranous nephropathy and hepatitis B virus infection

  Takekoshi. Hokkaido Igaku Zasshi. 1979
• **1988:** Strong association between IgA nephropathy and hepatitis B surface antigenemia in endemic areas

• 122 primary IgAN pt

• HBsAg was detected in 21 pt (17.2%)

• 9 / 21 failed to demonstrated any HBV antigens

**Table 2** Immunofluorescence/immunoperoxidase studies for HBV antigens in renal biopsies.

<table>
<thead>
<tr>
<th>Patient number</th>
<th>IgA</th>
<th>IgG</th>
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<th>Glom HBsAg</th>
<th>Glom HBeAg</th>
<th>Glom HBV DNA</th>
<th>Tubular HBV DNA</th>
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</table>

All glomeruli showed predominant mesangial IgA immunofluorescence (IF). The IgG and IgM IF were located in the mesangium with the exception of three biopsies* that showed additional granular capillary IgG deposition.

Abbreviations: ND – not done, Glom – glomerular.
• 1990: Membranoproliferative glomerulonephritis with semilunar forms and massive deposits of IgA associated with HBsAg

Toblli JE et al., Medicina (B Aires). 1990
1991: Membranous Nephropathy related to Hepatitis B virus in Adults

- Patients No.: 21
- Course of HBV-related membranous nephropathy in adults in areas where HBV is endemic is not benign.
- 29% patients had progressive renal failure
- Regardless of treatment, the disease has a slowly but relentlessly progressive clinical course in ~ one third of patients.

• PAN is seen more frequently in North American and European patients and rarely in Asian patients.

• Acute renal failure in hepatitis B virus-related membranous nephropathy with mesangiocapillary transition and crescentic transformation, which partially responded to pulse methylprednisolone therapy, and subsequently recovered after plasma exchange.

Multiplication of HBV-DNA in the serum, the deposition of HBVAg in glomeruli of kidney increases, and the pathologic lesion aggravates, which have significant correlation.

- Higher the HBVDNA level, more the deposition of HBV antigens in glomeruli of kidney

Diagnosis

- Establishing a direct causative relationship between a virus and a specific kidney disease often is problematic

- Persistence of circulating HBV or HBV DNA

- Absence of other causative agents

- Presence of HBV-specific antigen(s) or viral genome in the glomerulus
Dx & Assessment of response to treatment

- LFT
  - ALT, GGT, bilirubin levels

- HBV serologies
  - HBsAg, HBeAg, Anti-HBe, Anti-HBc

- Serum C3 & C4 levels
  - low in 20-50% patients
Treatment
HBV-induced glomerular disease

• Limited data (case series / uncontrolled observations)
IS + steroid / PE

• Little benefit.

• Immunosuppressive therapy may
  – increase viral replication
  – possibly lead to exacerbation of chronic hepatitis

• particularly when it is withdrawn

Lai KN et al. Nephron 1990
Sayarlioglu, H et al. Ann Pharmacother 2005
Anti-viral agents

- Interferon alfa
- Lamivudine
- Adefovir
- ? Entecavir
Adenine arabinoside and thymic extract

• Patient No. 24
• HBV MN patients who had previously received corticosteroid treatment and had persistent proteinuria [heavy (22 of 24, 91.6%) or mild (2 of 24, 8.4%)].

• Treatment: combination therapy with adenine arabinoside for two weeks and thymic extract (Thymostimulin) for six months to decrease urine protein loss and obtain seroconversion.

• Results: only one case (4.2%) had heavy and two cases (8.4%) mild proteinuria;

Lin CY et al., Kidney Int. 1991
Antiviral agent

- **1989:**
- A 9-year-old boy with hepatitis B-associated glomerulonephritis and nephrotic syndrome
- Treatment: antiviral combination therapy including interferon and acyclovir.
- Result: Improvement

De Man RA et al. J Hepatol. 1989
Interferon alfa

- The clinical response to therapy with interferon alfa was disappointing;
- Only one of the five patients treated had a complete remission with seroconversion to antibody to HBeAg.

Interferon alfa

- Long-term remission in liver disease in 8 of 15 patients with chronic hepatitis B and glomerulonephritis.

- Significant improvement in markers of renal disease in the majority of patients.

Conjeevaram HS et al. Gastroenterology 1995
Interferon alfa

- 4-8 months Interferon alfa therapy:
  - sustained HBeAg clearance: 38-80%
  - remission of proteinuria: 25-100%

Lin CY et al. Kidney Int 1995
Conjeevaram HS et al. Gastroenterology 1997
Interferon

• Interferon is less well tolerated but is more likely to induce a prolonged remission.

• In younger patients without renal impairment, a course of interferon, or pegylated interferon, may be an alternative.
Lamivudine

• 2003:
  • HBV associated nephrotic syndrome: resolution with oral lamivudine.
    Connor FL et al., Arch Dis Child. 2003

• Numerous case reports
Lamivudine

- Biopsy proven membranous nephropathy associated with HBV patient No. : 10
- Historic controls No: 12
- QMH, UCH
- Lamivudine was available in Hong Kong in 1998

Tang S et al. Kidney Int 2005
ESRD: 2 received renal transplantation and 3 were established on peritoneal dialysis. Those who progressed to ESRD had higher mean baseline proteinuria (3.6 ± 0.37 g/24 hours in nonprogressors vs. 5.0 ± 0.87 g/24 hours in progressors, \( P = 0.007 \)). Other factors that may predict progression to ESRD were not identified. The remaining patients without ESRD, who were followed for a mean of 181 ± 88 months, continued to have fluctuating levels of ALT (Fig. 4) and proteinuria, although the intergroup difference in ALT was not statistically significant. Three patients lost HBsAg, 2 of whom developed anti-HBc (Table 2).

The cumulative 3-year renal survival was 100% in group 1 and 58% in group 2 (\( P = 0.024 \), log-rank test) (Fig. 5). Change in serum creatinine over time was shown in Figure 6. Treatment with lamivudine was associated with a 41% reduction in the actual risk of progression to ESRD within 3 years, and a protection odds ratio of 7.3 (95% CI 0.7–81). Hepatic decompensation or malignancy was not observed during follow-up in both groups.
Table 2. HBV c-sequences and clinical remission status in all subjects

<table>
<thead>
<tr>
<th>Subject #</th>
<th>At Baseline</th>
<th>At 12 months</th>
<th>At 36 months</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>HBeAg</td>
<td>Anti-HBe</td>
<td>HBeAg</td>
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<tr>
<td>Group 1</td>
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Group 2

<table>
<thead>
<tr>
<th>Subject #</th>
<th>At Baseline</th>
<th>At 12 months</th>
<th>At 36 months</th>
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<tbody>
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<td>Anti-HBe</td>
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Abbreviations are: CR, complete remission of proteinuria (<0.3 g/24 hrs); PR, partial remission of proteinuria (≥50% reduction from baseline, but exceeding 0.3 g/24 hrs); NR, no remission of proteinuria; ESRD, end-stage renal disease.

<sup>a</sup>Lamivudine was stopped after 2 years' treatment.

<sup>b</sup>Absolute ALT level below upper limit of normal range.
Fig. 5. Kaplan-Meier analysis of renal survival in patients who received (solid line) and did not receive (dotted line) lamivudine treatment for HBV-associated MN.
• Treatment with lamivudine
  – disappearance of HBV DNA
  – substantial reduction of proteinuria
  – Six of 10 treated and 3 of 12 control patients had remission of proteinuria to <0.3 g/d.

• Conclusion: Lamivudine treatment improves renal outcome in HBV carriers with MN and evidence of liver disease.

  Tang S et al. Kidney Int 2005
Table 1. Baseline characteristics of clinical trials included in the analysis

<table>
<thead>
<tr>
<th>Authors</th>
<th>Country</th>
<th>Patients, n</th>
<th>Study design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lai et al.(^{22})</td>
<td>Hong Kong</td>
<td>5</td>
<td>Co, P</td>
</tr>
<tr>
<td>Lin(^{23})</td>
<td>Taiwan</td>
<td>20</td>
<td>CCT</td>
</tr>
<tr>
<td>Conjeevaram et al.(^{24})</td>
<td>US</td>
<td>15</td>
<td>Co, R</td>
</tr>
<tr>
<td>Chung et al.(^{25})</td>
<td>Korea</td>
<td>8</td>
<td>Co, P</td>
</tr>
<tr>
<td>Bhimma et al.(^{26})</td>
<td>South Africa</td>
<td>24</td>
<td>CCT</td>
</tr>
<tr>
<td>Tang et al.(^{27})</td>
<td>China</td>
<td>10</td>
<td>CCT</td>
</tr>
</tbody>
</table>

R, retrospective; P, prospective; Co, cohort study; CCT, clinical controlled study.
Baseline characteristics of clinical trials: clinical and histologic data

<table>
<thead>
<tr>
<th>Authors</th>
<th>Male, n</th>
<th>Mean age, years</th>
<th>MN, n</th>
<th>MPGN, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lai <em>et al.</em>(^{22})</td>
<td>100% (5/5)</td>
<td>27.2 ± 6.2</td>
<td>100% (5/5)</td>
<td>0</td>
</tr>
<tr>
<td>Lin(^{23})</td>
<td>75% (15/20)</td>
<td>6.2 ± 2.4</td>
<td>100% (20/20)</td>
<td>0</td>
</tr>
<tr>
<td>Conjeevaram <em>et al.</em>(^ {24})</td>
<td>86% (13/15)</td>
<td>39</td>
<td>66.6% (10/15)</td>
<td>26.6% (4/15)</td>
</tr>
<tr>
<td>Chung <em>et al.</em>(^ {25})</td>
<td>100% (8/8)</td>
<td>40.1</td>
<td>25% (2/8)</td>
<td>50% (4/8)</td>
</tr>
<tr>
<td>Bhimma <em>et al.</em>(^ {26})</td>
<td>89.4% (17/19)</td>
<td>8.7</td>
<td>79.2% (19/24)</td>
<td>4.2% (1/24)</td>
</tr>
<tr>
<td>Tang <em>et al.</em>(^ {27})</td>
<td>70% (7/10)</td>
<td>48.3 ± 12.8</td>
<td>100% (10/10)</td>
<td>0</td>
</tr>
</tbody>
</table>

MN, membranous glomerulonephritis; MPGN, membranoproliferative glomerulonephritis.
Meta-analysis: anti-viral therapy of hepatitis B virus-associated glomerulonephritis

<table>
<thead>
<tr>
<th>Authors</th>
<th>IFN dose, MU</th>
<th>IFN duration, months</th>
<th>Follow-up, months</th>
<th>Anti-viral therapy, type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lai et al.(^{22})</td>
<td>3 × 3/week</td>
<td>4</td>
<td>12</td>
<td>r-IFN(\alpha) 2b</td>
</tr>
<tr>
<td>Lin(^{23})</td>
<td>5 × 3/week</td>
<td>12</td>
<td>12</td>
<td>r-IFN(\alpha) 2b</td>
</tr>
<tr>
<td>Conjeevaram et al.(^{24})</td>
<td>5 × 7/week</td>
<td>4</td>
<td>43.2</td>
<td>r-IFN(\alpha) 2b</td>
</tr>
<tr>
<td>Chung et al.(^{25})</td>
<td>3 × 3/week</td>
<td>6</td>
<td>6 (6–16)</td>
<td>r-IFN(\alpha) 2b</td>
</tr>
<tr>
<td>Bhimma et al.(^{26})</td>
<td>10 × 3/week</td>
<td>4</td>
<td>6</td>
<td>r-IFN(\alpha) 2b</td>
</tr>
<tr>
<td>Tang et al.(^{27})</td>
<td>100 mg/day*</td>
<td>49.2 ± 16.5*</td>
<td>NA</td>
<td>Lamivudine</td>
</tr>
</tbody>
</table>

* Lamivudine dose and lamivudine duration of therapy. IFN, interferon; NA, information needed not available.
Meta-analysis: anti-viral therapy of hepatitis B virus-associated glomerulonephritis

Outcome of clinical trials

<table>
<thead>
<tr>
<th>Authors</th>
<th>HBsAg clearance</th>
<th>Sustained HBsAg clearance</th>
<th>HBeAg clearance</th>
<th>Sustained HBeAg clearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lai et al.</td>
<td>0</td>
<td>0</td>
<td>20% (1/5)</td>
<td>20% (1/5)</td>
</tr>
<tr>
<td>Lin</td>
<td>60% (12/20)</td>
<td>55% (11/20)</td>
<td>80% (16/20)</td>
<td>80% (16/20)</td>
</tr>
<tr>
<td>Conjeevaram et al.</td>
<td>33.3% (5/15)</td>
<td>33.3% (5/15)</td>
<td>66.6% (10/15)</td>
<td>53.3% (8/15)</td>
</tr>
<tr>
<td>Chung et al.</td>
<td>0</td>
<td>0</td>
<td>62.5% (5/8)</td>
<td>37.5% (3/8)</td>
</tr>
<tr>
<td>Bhimma et al.</td>
<td>0</td>
<td>0</td>
<td>58.3% (14/24)</td>
<td>41.6% (10/24)</td>
</tr>
<tr>
<td>Tang et al.</td>
<td>0</td>
<td>NA</td>
<td>50% (5/10)</td>
<td>NA</td>
</tr>
</tbody>
</table>

HBsAg, hepatitis B surface antigen; HBeAg, hepatitis B e antigen; NA, information needed not available.
## Meta-analysis: anti-viral therapy of hepatitis B virus-associated glomerulonephritis

### Outcome of clinical trials

<table>
<thead>
<tr>
<th>Authors</th>
<th>Proteinuria, remission (%)</th>
<th>Proteinuria, sustained remission (%)</th>
<th>Drop-out rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lai et al.(^{22})</td>
<td>80% (4/5)</td>
<td>20% (2/5)</td>
<td>0</td>
</tr>
<tr>
<td>Lin(^{23})</td>
<td>100% (20/20)</td>
<td>100% (20/20)</td>
<td>0</td>
</tr>
<tr>
<td>Conjeevaram et al.(^{24})</td>
<td>66.6% (10/15)</td>
<td>53.3% (8/15)</td>
<td>0</td>
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<td>Chung et al.(^{25})</td>
<td>37.5% (3/8)</td>
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<td>62.5% (15/24)</td>
<td>41.6% (10/24)</td>
<td>20.8% (5/24)</td>
</tr>
<tr>
<td>Tang et al.(^{27})</td>
<td>70% (7/10)</td>
<td>NA</td>
<td>0</td>
</tr>
</tbody>
</table>

NA, information needed not available.

F Fabrizi et al. Aliment Pharmacol Ther 2006
Adefovir dipivoxil

- **OBJECTIVE:** To investigate the efficacy and safety of adefovir dipivoxil (ADV) in treating hepatic cirrhosis complicated with hepatitis B virus associated glomerulonephritis.

- **Patient No.: 6**

- **RESULTS:**
  - After 3 and 6 months treatment:
    - negative conversion rates of HBV-DNA were 33.3% and 83.3%;
    - negative conversion rates of HBeAg were 16.7% and 66.7%;
    - positive conversion rates of HBeAb were both 16.7%;
    - recovery rates of ALT were 83.3% and 100.0%;
    - recovery rates of TBil were 66.7% and 83.3% respectively.
    - Protein in the urine of two patients was decreased to 0.3 g/d and in three patients it was 50% of the original values.

- After 1 year treatment:
  - Disease subsided fully in 3 and partially in 2 patients.

- **CONCLUSION:** Treating hepatic cirrhosis complicated with hepatitis B virus associated glomerulonephritis using adefovir dipivoxil is effective and safe.

Li DF et al. Zhonghua Gan Zang Bing Za Zhi. 2008
Entecavir

• Mechanism of action: -
  – Inhibits reverse transcriptase;
  – Incorporates into viral DNA (nucleoside reverse transcriptase inhibitor)

• No data
• Optimal duration of antiviral treatment is unclear

• Many patients will require prolonged treatment.

• Antiviral medications with low risk of resistance are preferred.
• Whether combination therapy will be better remains to be determined.
Lamivudine Vs Entecavir

• Lamivudine:-
  – Greatest experience
  – Anecdotal reports of improvement in proteinuria and renal outcomes
  – Disadvantage: the high rate of resistance developing with prolonged use (from treatment experience of HBV disease in general).

• Entecavir:-
  – may be preferred if long-term therapy is expected
  – from experience of recent advance of treatment of HBV disease.