Update on Hepatitis B and Hepatitis C

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Introduction

- Set up in Bradford
- Hepatitis B
- Hepatitis C
Introduction

- Set up in Bradford
- Hepatitis B
- Hepatitis C
Bradford Gastroenterology Department

- Catchment area: 500,000
- Tertiary referral: 1,000,000
- 6 consultants
  - 5 gastroenterologist
  - 1 hepatologist
My Team

- 1 Specialist Registrar
- 1 FY2 – SHO
- 2 FY1’s – House Officers
- 2 Viral Hepatitis Nurses
- 1 Alcohol Nurse
My Job

- **Acute Medicine**
  - Deputy Clinical Director of Acute Medicine
  - 800 in-patients

- **Gastroenterology**
  - 3 endoscopy lists
    - 580 OGD’s,
    - 159 sigmoidoscopies,
    - 215 colonoscopies

- **Hepatology**
  - 431 new patients, 2000 follow ups (17% DNA’s)
Research

– On a shoe string!
Introduction

- Set up in Bradford
- Hepatitis B
- Hepatitis C
Hepatitis B

- Why is hepatitis B important?
- Recent changes in treatment.
- Hepatitis B in Bradford.
Hepatitis B virus (HBV)

- Member of *Hepadnaviridae* that primarily infects liver cells\(^1\)
- WHO: ‘HBV is second only to tobacco as a known human carcinogen’\(^2\)
- 100 times more infectious than HIV\(^3\)
- 10 times more infectious than HCV\(^3\)

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1. NIH 11\(^{th}\) Report on Carcinogens, 2004;
2. Department of Communicable Diseases Surveillance and Response; WHO. Hepatitis B. 2002
3. DC. MMWR. 2003;52(RR01):1-33
The global impact of HBV disease

- World population: ~6 billion
- 2 billion with evidence of HBV infection
- 350–400 million with chronic hepatitis B
- 25–40% die of cirrhosis or liver cancer

References:
4. WHO, Fact sheet No. 204;
5. Conjeevaram HS, Lok AS. J Hepatol. 2003;38:S90-103
Chronic infection prevalence
- ≥8% – High
- 2–7% – Intermediate
- <2% – Low

Lifetime HBV infection risk
- >60%
- 20–60%
- <15%

Predominant age at infection
- Perinatal and early childhood
- Early childhood
- Adult

7. Adapted from CDC Hepatitis B slide set
Why do we need to treat Hepatitis B?

Chronic Infection

Liver cancer (HCC)

5-10% 9

25-40% lifetime risk for death due to HCC or liver failure 6

Liver Transplantation

Liver failure

23% in 5 yr 10

25-40% lifetime risk for death due to HCC or liver failure 6

Liver Transplantation

Cirrhosis

30% 9

25-40% lifetime risk for death due to HCC or liver failure 6

Liver Transplantation

Acute flare

10-15% in 5 yr 8

Death

Adapted from:
REVEAL: High HBV viral load associated with increased incidence of cirrhosis

All participants (n=3,582)

Baseline HBV DNA level (copies/mL)
- ≥10^6
- 10^5–<10^6
- 10^4–<10^5
- 300–<10^4
- <300

Cumulative incidence liver cirrhosis

Year of follow-up

P value for log-rank test, <0.001

13. Adapted from Iloeje UH, et al. Gastroenterology. 2006;130:678–86
Benefit of treatment in cirrhotic patients with chronic hepatitis B

Kaplan-Meier estimate of time to disease progression

- Placebo (n=215)
- LVD treated:
  - M204I/V mutations (n=209, 49%)
  - Wild-type (n=221)

Patients with disease progression (%)

Time after randomisation (months)

What’s important in the management of hepatitis B?
Hepatitis B
Hepatitis B

Diagnosis: HepBsAg
Hepatitis B

**Diagnosis**
- HepBsAg

**Markers**
- eAg positive
- eAg negative
# Hepatitis B

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>HepBsAg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Markers</td>
<td>eAg positive or eAg –ve</td>
</tr>
<tr>
<td>Viral load</td>
<td>Cut off</td>
</tr>
<tr>
<td></td>
<td>eAg +ve &gt;20000 IU/ml</td>
</tr>
<tr>
<td></td>
<td>eAg –ve &gt;2000 IU/ml</td>
</tr>
</tbody>
</table>
# Hepatitis B

**Diagnosis**  
HepBsAg

**Markers**  
eAg positive or eAg –ve

**Viral load**  
Cut off  
eAg +ve >20000 IU/ml  
eAg –ve >2000IU/ml

**ALT**  
Normal or raised
How best to treat chronic HBV?
Available guidelines 2004

- **EASL** 2003
  - J Hepatol 2003;39:S3-25

- **AASLD** 2004

- **US Treatment algorithm** 2004
Leeds-Bradford guidelines 2004

Liver Biopsy

Necroinflam < 4
Fibrosis < 3

No therapy
→ 6/12 follow-up

Necroinflam > 4
And/or fibrosis 3/4

Start treatment
by consultant

Monitoring 3 monthly for first year, then 6 monthly
- LFTs
- HBV markers
- Viral Load

IFN – set treatment protocol.

For lamivudine, continue lamivudine for 6 months after seroconversion and PCR undetectable.
Stop lamivudine if seroconversion maintained. Monitor patient 6 monthly.
If patient relapses, restart treatment.

If no seroconversion continue lamivudine indefinitely.

Cirrhosis
Fibrosis 5/6

Start treatment with lamivudine

Monitoring 3 monthly
- LFTs
- Viral load
See text
Clinic follow-up for patients on Lamivudine therapy

ALT monthly for three months, initially and 3-monthly afterwards, then 6 monthly. Test serum HBeAg, anti-HBe, HBV-DNA every 6 months.

- HBeAg-ve
  - Anti-HBe-ve
    - Seroconversion
      - Stop Lamivudine
      - After a further 6 mo
    - Continue Lamivudine
  - Anti-HBe-ve
    - Continue Lamivudine

- HBeAg-ve
  - ALT normal
    - Continue Lamivudine
  - ALT elevated
    - 2-3xULN or ≥500 IU/L
      - Assume YMDD mutation
      - Add Adefovir

*ALT elevation on Lamivudine can be spontaneous fluctuations, seroconversion, emergence of resistant species. If ALT > pre-treatment level consider stopping treatment if < pre-treatment, then continue.

Clinic follow-up after stopping Lamivudine therapy:
Test serum ALT, HBs, and HB DNA monthly for 4 months if
- ALT remains normal, HBeAg-ve and anti-HBe-ve then annual follow-up
- ALT elevated, HBeAg-ve or Anti-HBe-ve monitor 3 monthly

NB: Post treatment flares are often asymptomatic, not uncommon (14%) and may have no significance.
## Leeds-Bradford guidelines 2004

<table>
<thead>
<tr>
<th>HBeAg</th>
<th>HBV DNA &gt; 10^5 copies/ml</th>
<th>ALT</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>+</td>
<td>&lt; x1.5</td>
<td>Observe</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>&gt; x1.5</td>
<td>Lamivudine min 1 yr Continue 3-6 mo after seroconversion*</td>
</tr>
<tr>
<td>-Ag</td>
<td>+</td>
<td>&gt; x1.5</td>
<td>Lamivudine until PCR negative*</td>
</tr>
<tr>
<td>-Ag</td>
<td>-Ag</td>
<td>&lt; x1.5</td>
<td>Observe</td>
</tr>
<tr>
<td>+/-</td>
<td>+/-</td>
<td>cirrhosis</td>
<td>Comp: Lamivudine Decomp: lamivudine &amp; work-up for OLT</td>
</tr>
</tbody>
</table>

### AASLD guidelines (Lok 2004)
- The aim of Rx is durable suppression of HBV DNA to the lowest possible level.
- The endpoint of Rx is seroconversion from eAg positive to eAb positive.
- For Lamivudine monitoring see text.
- * Add Adefovir if resistance develops to lamivudine (DNA rises during treatment) and continue indefinitely. Genetic sequencing may be requested to confirm resistance.

### Efficacy of HBV treatment

<table>
<thead>
<tr>
<th></th>
<th>Lamivudine</th>
<th>IFN alpha 2b</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 1 year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DNA loss</td>
<td>44%</td>
<td>37%</td>
</tr>
<tr>
<td>eAg loss</td>
<td>32%</td>
<td>33%</td>
</tr>
<tr>
<td>Seroconversion</td>
<td>100% (50% at 5 yr)</td>
<td>18%</td>
</tr>
<tr>
<td>Durability of seroconv</td>
<td>77% at 37 mo</td>
<td>90% at 8 yrs</td>
</tr>
<tr>
<td>eAg loss</td>
<td>n/a</td>
<td>11%</td>
</tr>
<tr>
<td>ALT normalisation</td>
<td>40-70%</td>
<td>23%</td>
</tr>
<tr>
<td>Histol improvement</td>
<td>50%</td>
<td>90%</td>
</tr>
<tr>
<td>Resistance</td>
<td>14.32% (69% at 5 yr)</td>
<td>Nil</td>
</tr>
</tbody>
</table>
How best to treat chronic HBV? Available guidelines 2007

- **EASL** 2003
  - J Hepatol 2003;39:S3-25

- **AASLD** 2004

- **Treatment algorithm** 2004

- **APASL** 2006
  - Liver Int 2006;26:47-58

- **US algorithm** 2006

- **AASLD** 2007

- **NICE** 2006
Management of chronic HBV

**NOTE:**
- When considering treatment of HBV the ULN for ALT should be considered to be <19 for women and <30 for men
- HBV DNA results are given in IU/ml, older results and results from other hospitals may be in copies/ml (to convert from copies/ml to IU/ml, divide by 5)
- Note the different cut off in HBV DNA between eAg POS and eAg NEG patients

<table>
<thead>
<tr>
<th>HBeAg</th>
<th>HBV DNA (IU/ml)</th>
<th>ALT</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>POS</td>
<td>&lt;20,000</td>
<td>Persistently normal</td>
<td>6 monthly reviews initially, then annual review</td>
</tr>
<tr>
<td>POS</td>
<td>&gt;20,000</td>
<td>Persistently normal</td>
<td>Low efficacy with current treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;2x ULN</td>
<td>Repeat LFTs 3 monthly initially and consider biopsy if ALT rises, if family history of HCC or patient age &gt;40</td>
</tr>
<tr>
<td>POS</td>
<td>&gt;20,000</td>
<td>1–2x ULN</td>
<td>Consider liver biopsy to determine if ongoing inflammation/fibrosis, otherwise initial 3 monthly LFTs and biopsy if ALT rises to 2x ULN</td>
</tr>
<tr>
<td>POS</td>
<td>&gt;20,000</td>
<td>≥2x ULN</td>
<td>Will require treatment but consider biopsy to stage disease</td>
</tr>
<tr>
<td>NEG</td>
<td>&lt;2,000</td>
<td>Persistently normal</td>
<td>Observe with repeat LFTs and HBV DNA, biopsy if HBV DNA rise</td>
</tr>
<tr>
<td>NEG</td>
<td>&lt;2,000</td>
<td>1–2x ULN</td>
<td>3 monthly LFTs and if ALT rises further for liver biopsy</td>
</tr>
<tr>
<td>NEG</td>
<td>&lt;2,000</td>
<td>≥2x ULN</td>
<td>Consider liver biopsy to determine if ongoing inflammation/fibrosis</td>
</tr>
<tr>
<td>NEG</td>
<td>2,000–20,000</td>
<td>Persistently normal</td>
<td>3 monthly LFTs and if LFTs become abnormal then liver biopsy</td>
</tr>
<tr>
<td>NEG</td>
<td>&gt;20,000</td>
<td>&gt;2x ULN</td>
<td>Will probably require treatment but consider liver biopsy to determine extent of inflammation/fibrosis</td>
</tr>
</tbody>
</table>
Hepatitis B - management

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<thead>
<tr>
<th>Marker</th>
<th>Viral load IU/ml</th>
<th>ALT</th>
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<tbody>
<tr>
<td>eAg +ve</td>
<td>&lt;20 000</td>
<td>Normal</td>
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<td>Raised</td>
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</tr>
<tr>
<td>eAg +ve</td>
<td>&gt;20000</td>
<td>Raised</td>
<td>Biopsy and treat</td>
</tr>
<tr>
<td>eAg -ve</td>
<td>&lt;2000</td>
<td>Normal</td>
<td></td>
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<td>Normal</td>
<td></td>
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<tr>
<td>eAg -ve</td>
<td>&gt;2000</td>
<td>Raised</td>
<td>Biopsy and treat</td>
</tr>
</tbody>
</table>
Hepatitis B - Treatment

- No treatment to eradicate hepatitis B
- Treatment aims to keep viral load low

Current treatment
- Lamivudine
- Adefovir
- Peg Interferon
- Entecavir
- Tenofovir
Hepatitis B - Treatment

- Fast acting medication
- Low resistance profile
HBV antiviral resistance

Lok ASF and McMahon BJ. Hepatology 2007;45(2):507-39
Current treatment

- Lamivudine 100mg od + Adefovir 10 mg od
- Pegylated interferon 180 mcg sc weekly – 48 weeks
- Entecavir 0.5mg od
- 3-6 monthly monitoring
Hepatitis B in Bradford

Extent of the problem to plan services.
Bradford population
2001 census

Total population\textsuperscript{18} 467 665

Ethnic minority\textsuperscript{19} 87 150 (18%)
  - Asian origin 75 050
  - Afro-Caribbean origin 5 950

Ethnic minority will rise to 26% by 2011\textsuperscript{19}

Estimated HBV patients

- Around 3–6% of first generation immigrants
- Assume 30,000
- Therefore, between 900–1800 HBV patients

Personal Communication – Dr Sulleman Moreea
HBV patients in Bradford

HBV patients 357

Males 157
- eAg +ve 35
  - ALT > 80 17
  - ALT < 80 12
- eAg –ve 122
  - ALT > 80 21
  - ALT < 80 64

Females 200
- eAg +ve 31
  - ALT > 80 5
  - ALT < 80 20
- eAg –ve 169
  - ALT > 80 5
  - ALT < 80 123

No data on 90 patients (25%)
# HBV in Bradford

<table>
<thead>
<tr>
<th>eAg status</th>
<th>ALT &lt;40</th>
<th>ALT 41-80</th>
<th>ALT &gt;80</th>
</tr>
</thead>
<tbody>
<tr>
<td>eAg +ve</td>
<td>11</td>
<td>10</td>
<td>18</td>
</tr>
<tr>
<td>VL &gt; 20000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>eAg +ve</td>
<td>9</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>VL &lt; 20000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>eAg –ve</td>
<td>30</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>VL &gt; 2000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>eAg –ve</td>
<td>121</td>
<td>24</td>
<td>11</td>
</tr>
<tr>
<td>VL &lt; 2000</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# HBV in Bradford

<table>
<thead>
<tr>
<th>eAg status</th>
<th>ALT &lt;40</th>
<th>ALT 41 - 80</th>
<th>ALT &gt;80</th>
</tr>
</thead>
<tbody>
<tr>
<td>eAg +ve VL &gt; 20000</td>
<td>11</td>
<td>10</td>
<td>18</td>
</tr>
<tr>
<td>eAg +ve VL &lt; 20000</td>
<td>9</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>eAg -ve VL &gt; 2000</td>
<td>30</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>eAg -ve VL &lt; 2000</td>
<td>121</td>
<td>24</td>
<td>11</td>
</tr>
</tbody>
</table>
## Patients on Treatment - 2008

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>16</td>
<td>7</td>
<td>23</td>
</tr>
<tr>
<td>LAM + ADV</td>
<td>5</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Pegasys</td>
<td>14</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>Entecavir</td>
<td>9</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>44</td>
<td>13</td>
<td>57</td>
</tr>
</tbody>
</table>
### Increase in work load

The results of our analysis are shown in Table 1.

<table>
<thead>
<tr>
<th>Viral load</th>
<th>eAg positive n = 25</th>
<th>eAg negative n = 122</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 20000 IU/ml</td>
<td>≥20000 IU/ml</td>
</tr>
<tr>
<td>ALT &gt; 40 IU/ml</td>
<td>1 (0M, 1F)</td>
<td>12 (0M, 1F)</td>
</tr>
<tr>
<td>ALT 30-40 IU/ml</td>
<td>4 (0M, 4F)</td>
<td>8 (1M, 7F)</td>
</tr>
<tr>
<td>ALT 60-80 IU/ml</td>
<td>0 (0M, 0F)</td>
<td>2 (0M, 2F)</td>
</tr>
<tr>
<td>Possible increase in liver biopsy numbers</td>
<td>N/A</td>
<td>67%</td>
</tr>
<tr>
<td>ALT &gt; 80 IU/ml</td>
<td>1 (0M, 1F)</td>
<td>10 (0M, 2F)</td>
</tr>
<tr>
<td>ALT 60-80 IU/ml</td>
<td>0 (0M, 0F)</td>
<td>2 (0M, 2F)</td>
</tr>
<tr>
<td>Possible increase in treated patients</td>
<td>N/A</td>
<td>20%</td>
</tr>
</tbody>
</table>

N/A = not applicable

# HBV patients – Ethnicity

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pakistanis</td>
<td>113</td>
<td>133</td>
<td>246 (70%)</td>
</tr>
<tr>
<td>White Caucasians</td>
<td>18</td>
<td>27</td>
<td>45 (13%)</td>
</tr>
<tr>
<td>Chinese</td>
<td>11</td>
<td>20</td>
<td>31 (8.6%)</td>
</tr>
<tr>
<td>African</td>
<td>11</td>
<td>19</td>
<td>30 (8.4%)</td>
</tr>
</tbody>
</table>

Personal Communication – Dr Sulleman Moreea
Prevalence of HBV in Bradford

- June 05 – Sep 06: 4817 pregnancies
  - 53% Asians
  - 42% Caucasians
  - 3% African
- 99% screened

Mahmood et al. BSG March 2008
Screening in pregnancy

- HBV positive pregnancies 42 (0.88%).
- Asians 29 (69%)
  - 23 of Pakistani origin, of whom
  - 11 born in Pakistan.
- White Caucasian 8 (19%)
- African 5 (12%)

Mahmood et al. BSG March 2008
Screening in pregnancy

Prevalence of HBV

- Asian 1.1%
- White Caucasian 0.4%
- African 3%

Mahmood et al. BSG March 2008
Screening in pregnancy

- eAg positive: 8 (19%)
- eAg negative: 34 (81%)

All of them were referred to the Hepatology clinic – 29/42 (69%) attended.

Mahmood et al. BSG March 2008
The large majority of Hepatitis B patients may not know they have the disease.

The morbidity and mortality due to Hepatitis B will be a problem in the future.
Set up in Bradford

Hepatitis B

Hepatitis C
  – What you need to know
  – Bradford experience
Outcome Following Hepatitis C Infection

Acute hepatitis C
55 - 85%
Chronic infection
70%
Chronic hepatitis
20%
Cirrhosis
1 - 4%/yr
HCC
4 - 5%/yr
Decompensation
### Prevalence In Groups at Risk

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipients of clotting factors before 1987</td>
<td>75 - 90%</td>
</tr>
<tr>
<td>Injection drug users</td>
<td>70 - 85%</td>
</tr>
<tr>
<td>Long-term hemodialysis patients</td>
<td>10%</td>
</tr>
<tr>
<td>Individuals with $\geq 50$ sexual partners</td>
<td>10%</td>
</tr>
<tr>
<td>Recipients of blood prior to 1990</td>
<td>5%</td>
</tr>
<tr>
<td>Infants born to infected mothers</td>
<td>5%</td>
</tr>
<tr>
<td>Long-term sexual partners of HCV positive</td>
<td>1 - 5%</td>
</tr>
<tr>
<td>Health workers after random needlesticks</td>
<td>1 - 2%</td>
</tr>
</tbody>
</table>

*CDC, MMWR 1998;47(No. RR-19):1*
Prevalence of HCV Infection Among Blood Donors

1.1-5% - Intermediate

>5% - High

0.2-1% - Low

≤0.1% - Very Low

Unknown

* Anti-HCV prevalence by EIA-1 or EIA-2 with supplemental testing; based on data available in January, 1995
HCV - Epidemiology

Epidemics From Parenteral Practices

- Japan: cupping
- Egypt: Schistosomiasis treatment
- Italy: home injections

Kiyosawa K et al., Gastroenterology 1994;106:1596
Frank C et al., Lancet 2000;355:877
Chiaramonte M et al., J Hepatol 1996; 24:129
HCV Treatment

Primary objective
- Viral eradication – SVR
- Arrest progression of necrosis/fibrosis

Secondary objective
- Reduce progression of fibrosis/cirrhosis
- Prevent decompensation
- Prevent HCC

SVR = sustained virological response
HCC = hepatocellular carcinoma
Evolution of hepatitis C treatment

Elucidation of HCV genome

Addition of RBV to IFN alfa improved outcomes

Peg-IFN alfa plus RBV becomes gold standard

1989

Treatment with IFN alfa for 24 or 48 weeks – 3x weekly dosing – Poor outcomes

Development of Peg-IFN – once-weekly dosing – Outcomes improved further

2006
Pegylated interferons lead to a significantly better treatment outcome.

Approved treatment duration is 48 weeks for genotype 1 and 24 weeks for genotype 2/3.

PEGASYS® 180 μg plus COPEGUS®

<table>
<thead>
<tr>
<th>Genotype 1</th>
<th>Genotype 2/3</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-LD</td>
<td>24-SD</td>
</tr>
<tr>
<td>29%</td>
<td>84%</td>
</tr>
<tr>
<td>42%</td>
<td>81%</td>
</tr>
<tr>
<td>41%</td>
<td>79%</td>
</tr>
<tr>
<td>52%</td>
<td>80%</td>
</tr>
</tbody>
</table>

n= 101 118 250 271 96 144 99 153

LD = RBV 800 mg/day
SD = RBV 1000–1200 mg/day

Prognosis and response to IFN-based treatment vary with baseline factors

- **Viral factors**
  - Genotype (1 and 4 versus 2 and 3)
  - Viral load (high versus low viral load)

- **Patient-specific factors**
  - Age
  - Liver histology (cirrhosis versus no cirrhosis)
  - Race
  - Body weight
  - Alcohol/drug use
  - Gender

---
1. Trepo C. J Viral Hepat 2000; 7: 250
2. Davis G & Lau G. Hepatology 1997; 26: 122S
Which Pegylated Interferon?

- Roche – Pegasys
  - Fixed dose

- Schering-Plough – Viraferon Peg
  - Weight-based
SVR: the 80% rule

- Retrospective analysis of pegIFN alfa-2b/RBV phase trials

Definitions of Response
Rapid virological response (RVR)
- Undetectable HCV RNA levels at week 4

Early virological response (EVR)
- $\geq 2 \log_{10}$ drop in HCV RNA at week 12

Slow virological response
- HCV RNA positive at weeks 4 and 12, negative at week 24

End-of-treatment response (EOT)
- Undetectable HCV RNA levels at end of treatment
  (24 weeks for HCV genotype 2/3, 48 weeks for HCV genotype 1)

Sustained virological response (SVR)
- Undetectable HCV RNA levels at end of treatment and follow-up
  (24 weeks post-treatment)

Rapid Virologic Response (RVR): HCV RNA Undetectable at Week 4

HCV RNA (log_{10} IU/mL) vs. Weeks

- PegIFN/RBV
- 2 log decline
- Limit of detection
- RVR
- SVR
Rapid Virologic Response (RVR): Super Responders

- HCV RNA (log_{10} IU/mL) over time
- PegIFN/RBV regimen
- RVR: 2 log decline
- Limit of detection
- SVR: Sustained Virological Response
Early Virologic Response (EVR):
HCV RNA ↓ ≥ 2 logs or Undetectable at Week 12
**Slow Virologic Response:**

HCV RNA Undetectable at Week 24

- PegIFN/RBV
- RVR
- EVR
- SVR

**HCV RNA (log10 IU/mL)**

- **Limit of detection**
- **2 log decline**

**Weeks**

-6 0 6 12 18 24 30 36 42 48 54 60 66 72 78
Slow Virologic Response:
Slow Responders

HCV RNA (log$_{10}$ IU/mL)

2 log decline

Limit of detection

RVR

EVR

Slow virologic response

SVR

-6 0 6 12 18 24 30 36 42 48 54 60 66 72 78

Weeks

PegIFN/RBV

Slow virologic response

2 log decline

Limit of detection

Weeks

-6 0 6 12 18 24 30 36 42 48 54 60 66 72 78
Null Response, Breakthrough and Relapse

- PegIFN/RBV
- HCV RNA (log_{10} IU/mL)
- Weeks
- SVR
- Limit of detection
- 2 log decline
- Breakthrough
- Null response
- Relapse
Treatment failure: definitions

Non-response

- Detectable HCV RNA levels at the end of treatment or end of follow-up

Breakthrough

- HCV RNA levels become undetectable during treatment, but virus reappears while still on treatment

Relapse

- HCV RNA negative at the end of treatment but subsequently positive during the follow-up period

Importance of EVR on SVR
Predictive value of RVR/EVR on SVR

- Retrospective analysis of genotype 1 patients receiving 48 weeks of pegIFN alfa-2a + RBV (N = 453)

Mathematical model – the Accordion Principle

G1 algorithm

Peginterferon + RBV 1000 or 1200 mg/day
Quantitative PCR at baseline

- ≤ 600,000 IU/mL
  - Qualitative PCR at week 4
    - (-) Treat for 24 weeks
    - (+) Treat for 48 weeks

- >600,000 IU/mL
  - Quantitative PCR at week 12
    - (-) ≥2-log drop
    - (<2-log drop Check at week 24
    - Stop
    - (+) Treat for 72 weeks
Who has Hepatitis C in the UK

- IV drug users? Prevalence
- People from high endemic areas
Problems in the UK

- Finding the patients
- Treatment
  - Cost
  - Side effects
Hepatitis C in the UK

- 466,000 people in the UK are infected with hepatitis C
- 86% of people infected are unaware of their status, putting others at risk
- Only 1 in 7 of those infected have been diagnosed
- 1-2% of people with hepatitis C are treated with NICE approved therapies
- Unless urgent action is taken, 116,000 people will develop liver cirrhosis

Hepatitis C Trust
Patients with HCV infection Nottingham Survey

Tested positive for anti-HCV

Referred for further investigation (49%)

Attend clinic appt (27%)

Undergo liver biopsy (17%)

Treated (10%)

Sustained response* (5%)

Not tested

Not referred (51%)

Do not attend (22%)

No liver biopsy (10%)

Not treated (7%)

Non-response/relapse (5%)

Data from S. Ryder for Trent Group
HCV burden in Bradford

Based on the national figures – at least 1750 cases in Bradford
HCV seen in the BRI - 2008

No of patients 500

Males 322
  - Caucasians 189
    - IVDU 175
  - Asians 131 (41%)
    - IVDU 13
  - Africans 2

Females 178
  - Caucasians 72
    - IVDU 66
  - Asians 104 (58%)
    - IVDU 2
  - Africans 2
# Genotypes

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>47</td>
<td>17</td>
<td>64</td>
</tr>
<tr>
<td>1b</td>
<td>26</td>
<td>11</td>
<td>37</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td>3a</td>
<td>120</td>
<td>82</td>
<td>202</td>
</tr>
<tr>
<td>3b</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>N/A</td>
<td>110</td>
<td>59</td>
<td>169</td>
</tr>
</tbody>
</table>
## Genotypes

<table>
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<th>Total</th>
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<td>169</td>
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</tbody>
</table>
Patients treated in Bradford

180 patients treated so far since 2005
Bradford – the community study

- DoH funded study in conjunction with London
- Mouth swabs from Asians in the community – mosques and community centres.
Bradford – the community study

1457 people from Oct 07 – Aug 08
– Aged 16 and over

Data from 1413 analysed
## Results

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>1413</td>
</tr>
<tr>
<td>males</td>
<td>1100</td>
</tr>
<tr>
<td>females</td>
<td>313</td>
</tr>
</tbody>
</table>

Alam S - Personal communication
### Results

#### Breakdown of different population groups

<table>
<thead>
<tr>
<th>Country/Ethnic group</th>
<th>Total</th>
<th>%</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pakistan</td>
<td>962</td>
<td>68%</td>
<td>769</td>
<td>193</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>112</td>
<td>8%</td>
<td>107</td>
<td>5</td>
</tr>
<tr>
<td>India</td>
<td>57</td>
<td>4%</td>
<td>51</td>
<td>6</td>
</tr>
<tr>
<td>Afghanistan</td>
<td>15</td>
<td>1%</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Burma</td>
<td>1</td>
<td>0.07%</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>UK (UK born asians)</td>
<td>266</td>
<td>19%</td>
<td>161</td>
<td>105</td>
</tr>
</tbody>
</table>
Results

Total
1413

Total Positives
65 (5%)

HBV Reactives
34 (2.6%)

HCV Reactives
31 (2.4%)

Total Negatives
1348

Alam S - Personal communication
### Results of Mouth Swabs

<table>
<thead>
<tr>
<th></th>
<th>HBV REACTIVE</th>
<th>HCV REACTIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Males</td>
</tr>
<tr>
<td></td>
<td>34</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>2.6%</td>
<td>2.1%</td>
</tr>
</tbody>
</table>

Alam S - Personal communication
Results

Total HCV Reactive
31

Blood Tested
20

HCV Ab +ve 5
HCV Ab –ve 15

Alam S - Personal communication
Results

Blood Test Results of subjects tested positive with mouth swab

- Total HBV Reactives: 34
- Blood Tested: 31
  - 19 HBsAg +ve
  - 12 HBsAg12-ve
    - All eAb +ve

Alam S - Personal communication
To conclude

There are a lot of similarities between Bradford and Mauritius.

The management of viral hepatitis is changing all the time – need for regular updates.