

# Use of liver biopsy in chronic hepatitis C & B

Aspects of NICE technology appraisals, 2006  
which are relevant to histopathologists

Jl Wyatt  
Nottingham, 2006

# Chronic hepatitis C

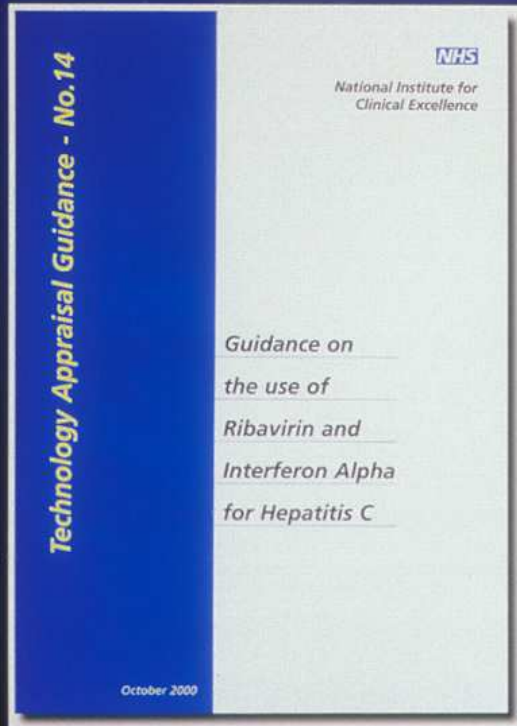
Aims of treatment:

to achieve sustained viral response

probably = cure

(90% not relapsed after 10 years)

# NICE Guidance on the use of ribavirin and interferon alpha for hepatitis C



Biopsy based treatment

Moderate to severe  
hepatitis C  
defined as histological evidence of

*significant scarring (fibrosis) and/or  
significant necrotic inflammation.*

*First NICE guidance October 2000*

*Reviewed January 2004 – retain biopsy based treatment;*

*may revise when results of mild hepatitis C studies are available*

*August 2006 – treatment of mild chronic hepatitis C*

# Peg IFN alfa and ribavirin for the treatment of mild chronic hepatitis C: (extension to previous guidance).

NICE Aug 2006

The same treatment with peg-Interferon and ribavirin is now recommended for patients with mild chronic hepatitis C.

= 6 months for genotypes 2&3, 1 year for type 1 and others

*'The decision to treat need not depend on a liver biopsy to determine the stage of the disease if treatment is initiated immediately.'*

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*'The decision to treat need not depend on a liver biopsy to determine the stage of the disease if treatment is initiated immediately.'*

*'However, a biopsy may be recommended by the clinician for other reasons or if a strategy of watchful waiting is chosen'.*

## Who will be biopsied?

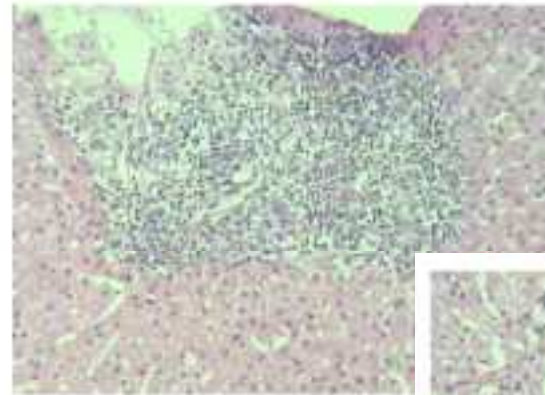
- patients who choose to defer treatment, e.g. genotype 1, to confirm disease is mild
- patients who may have dual pathology
- patients with clinically suspected cirrhosis,  
confirmation required for follow up, surveillance etc.

# What is mild disease?

- Absence of bridging fibrosis (less than this)



- Focal interface hepatitis, minority of portal tracts
- and  $<2$  foci of necroinflammatory activity per acinus



# Chronic hepatitis B

Aims of treatment:

to prevent cirrhosis and HCC

NICE technological appraisal 96:

## Adefovir dipivoxil and peginterferon alfa-2a for the treatment of chronic hepatitis B.

*February 2006*

### Treatments in succession

1. Initial treatment of adults with chronic hepatitis B  
= peginterferon alfa-2a
2. Treatment with IFN unsuccessful, poorly tolerated, or relapse
  - antiviral drugs lamivudine
  - resistance to lamivudine - adefovir

# Which patients with chronic hepatitis B to treat?

## - role of biopsy in chronic hepatitis B

**'IFN** for the treatment of *HBeAg-positive* or *HBeAg-negative* chronic hepatitis B in adults with compensated liver disease and

1. evidence of viral replication (*high HBV DNA level*),
2. high ALT and
3. *histologically verified liver inflammation and/or fibrosis.*

**Adefovir** – same but includes decompensated liver disease

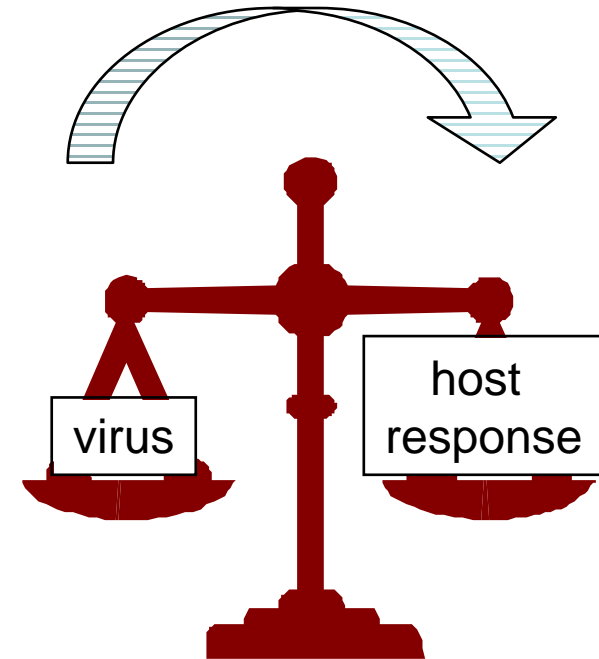
*Treatment not necessarily indicated for ALT x1.5-2 normal, low necroinflammatory score on biopsy'*

Chronic hepatitis B is a balance of virus against host immune response – treatment to tip balance in favour of the host

Treatments in succession (*not synergistic*)

Initial treatment of adults with chronic hepatitis B = peginterferon alfa-2a

Treatment with IFN unsuccessful, poorly tolerated,  
or relapse – antiviral drugs - lamivudine  
resistance to lamivudine - adefovir



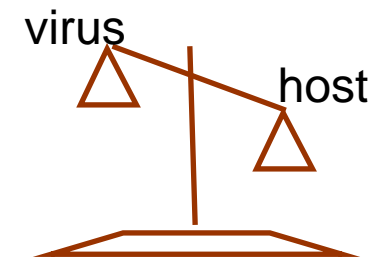
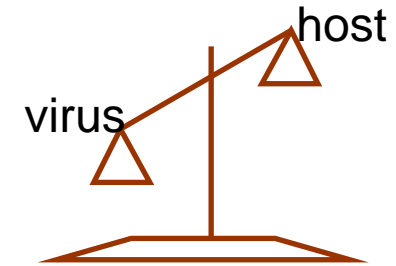
Boost inflammatory response

Weaken virus

# Phases of chronic hepatitis B

each may last many years

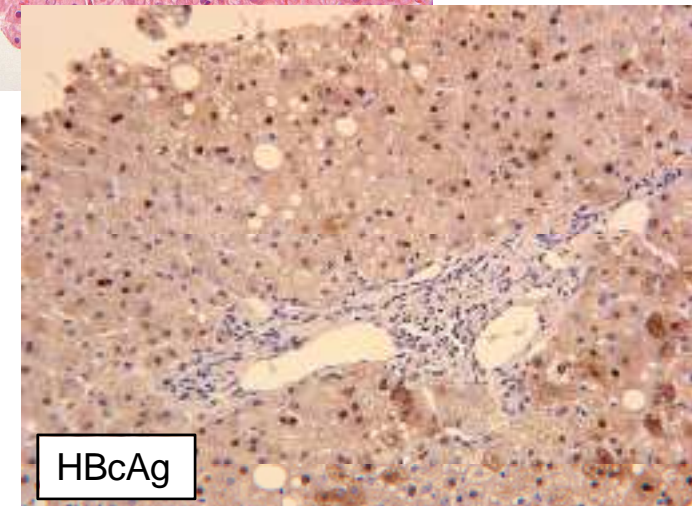
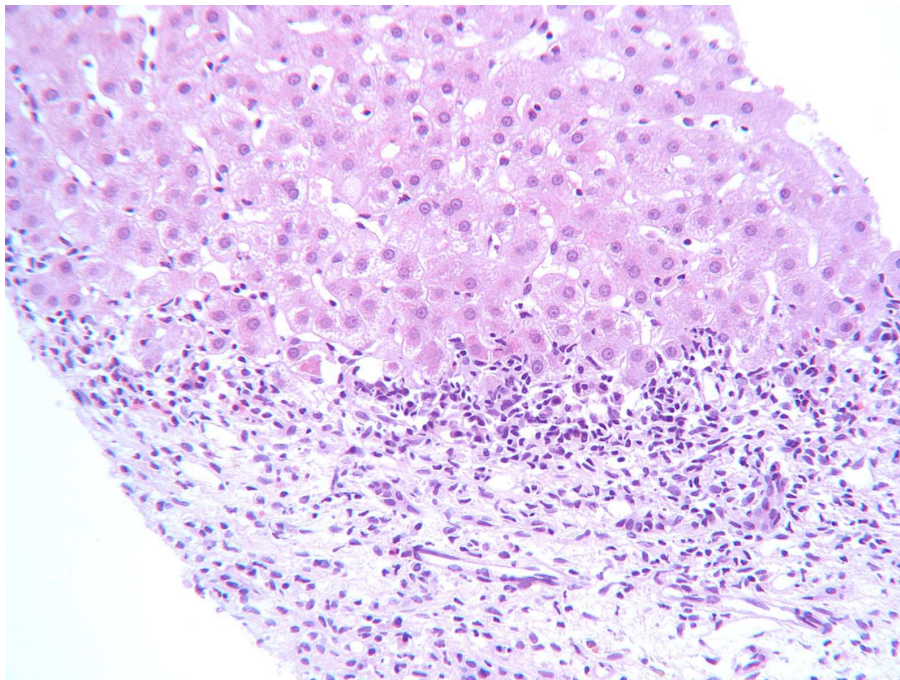
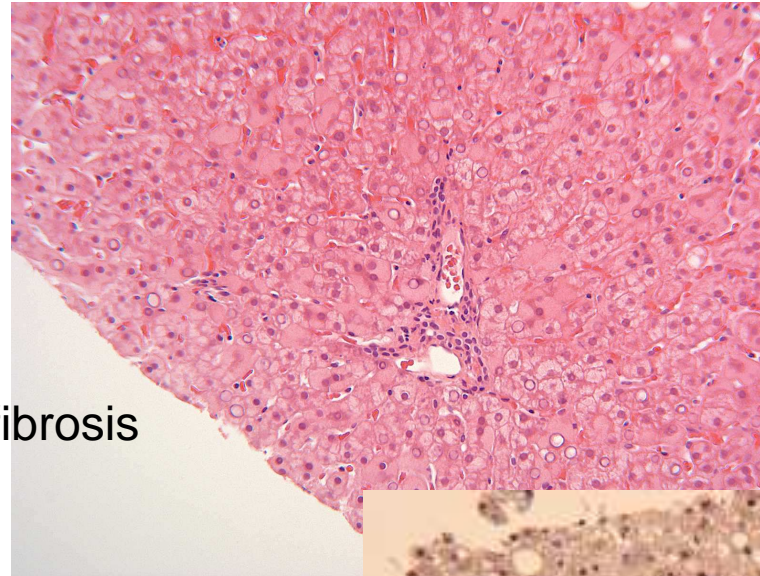
- 1. Immunotolerant phase - children**
  - High replication, infectious, no liver damage
  
- 2. Active chronic hepatitis B eAg +ve**
  - Immune system begins to fight virus
    - liver damage results, **cirrhosis 8-20% after 5 years**
  
- 3. HBeAg seroconversion 5-10% per year**
  - Flare of disease, get anti-HBeAb, good quality of life,
  - low risk of disease progression
  - = **Inactive HBsAg carrier state**



*Most stay in this state*

Immune tolerance  
Little/no inflammation  
Ground glass hepatocytes  
HBcAg +ve

Inactive HBsAg carrier state  
Mild portal inflammation, +/- fibrosis  
Ground glass hepatocytes  
HBcAg -ve



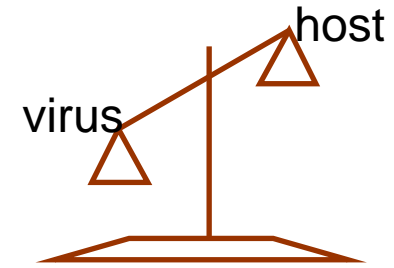
Active chronic  
Hepatitis B



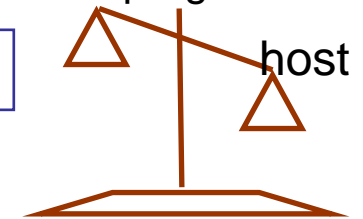
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*Most stay in this state*



*May then get*

## **HBsAg seroconversion**

- 0.5-2% per year in western countries. Rare in endemic countries.
- Follows HBeAg seroconversion, represents resolution of chronic infection (although may be 'occult hepatitis B')

*or*

## **HBeAg negative chronic hepatitis B**

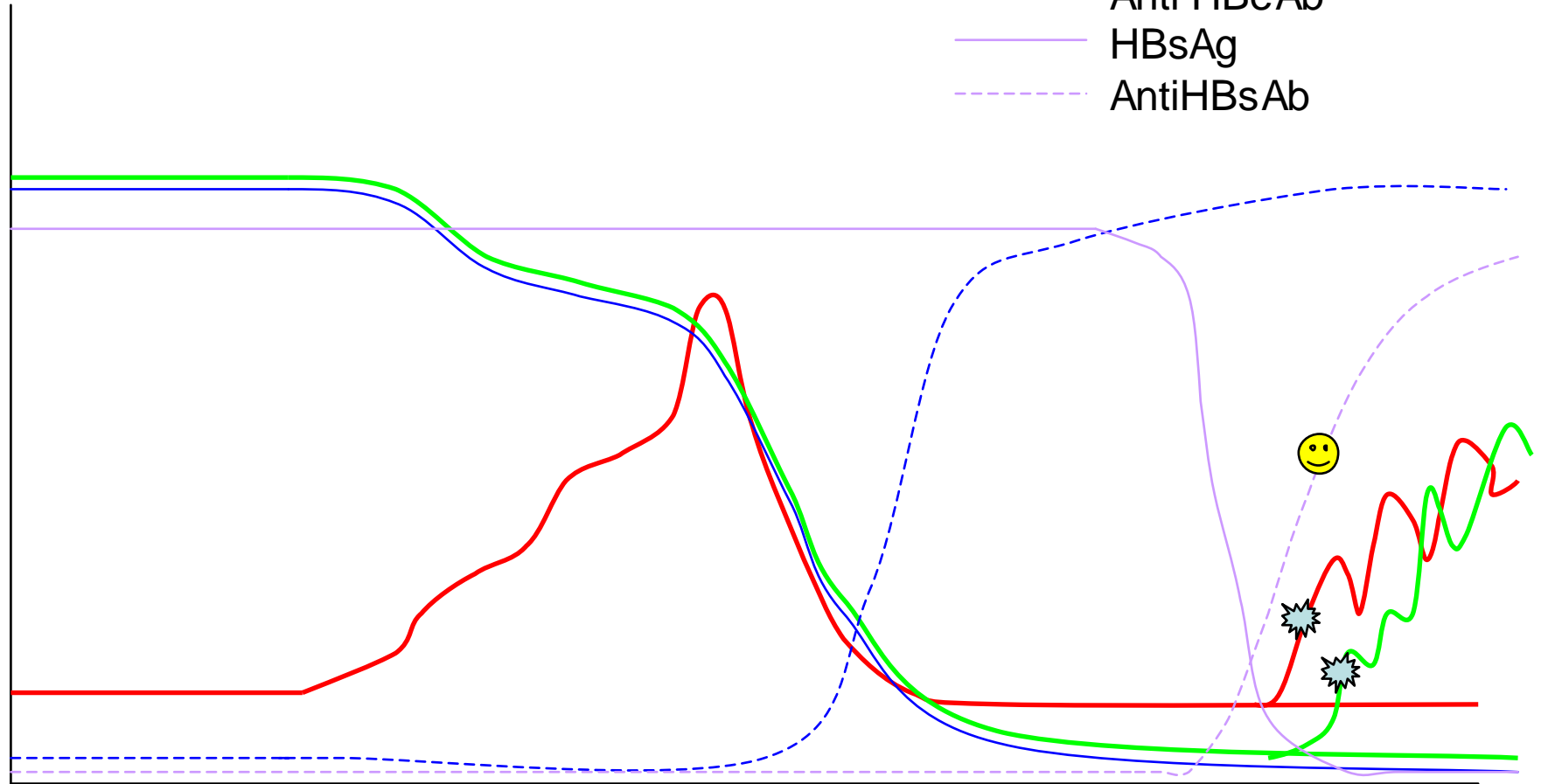
- Original infection or by mutation, fluctuating course and poor prognosis. Few achieve lasting remission with treatment.
- **Cirrhosis 8-10% per year.**



# Phases of chronic hepatitis B

each may last many years

- ALT
- HBV DNA
- HBeAg
- - - Anti HBeAb
- HBsAg
- - - AntiHBsAb



Immuno-tolerant phase

Active Chronic Hepatitis B  
Cirrhosis 8-20% in 5 years

HBeAg Serconversion  
 5-10%pa

*may then get*

😊 HBsAg Seroconversion  
 0.5-2% pa

or ⚡ HBeAg-ve Chronic hepatitis B  
Cirrhosis 8-10%pa

# Role of biopsy in chronic hepatitis B

= whether to treat, not what to use

*'Treat patients with high DNA  
and raised ALT  
and histologically verified liver  
inflammation and/or fibrosis.'*

*Treatment not necessarily indicated for ALT x1.5-2 normal, low necroinflammatory score on biopsy'*

Biopsy to show that raised ALT is due to chronic viral hepatitis and assess fibrosis/cirrhosis

In practice:

Wide variation in blood tests – ALT, antigens, antibodies, DNA

Clinical uncertainty – experts disagree

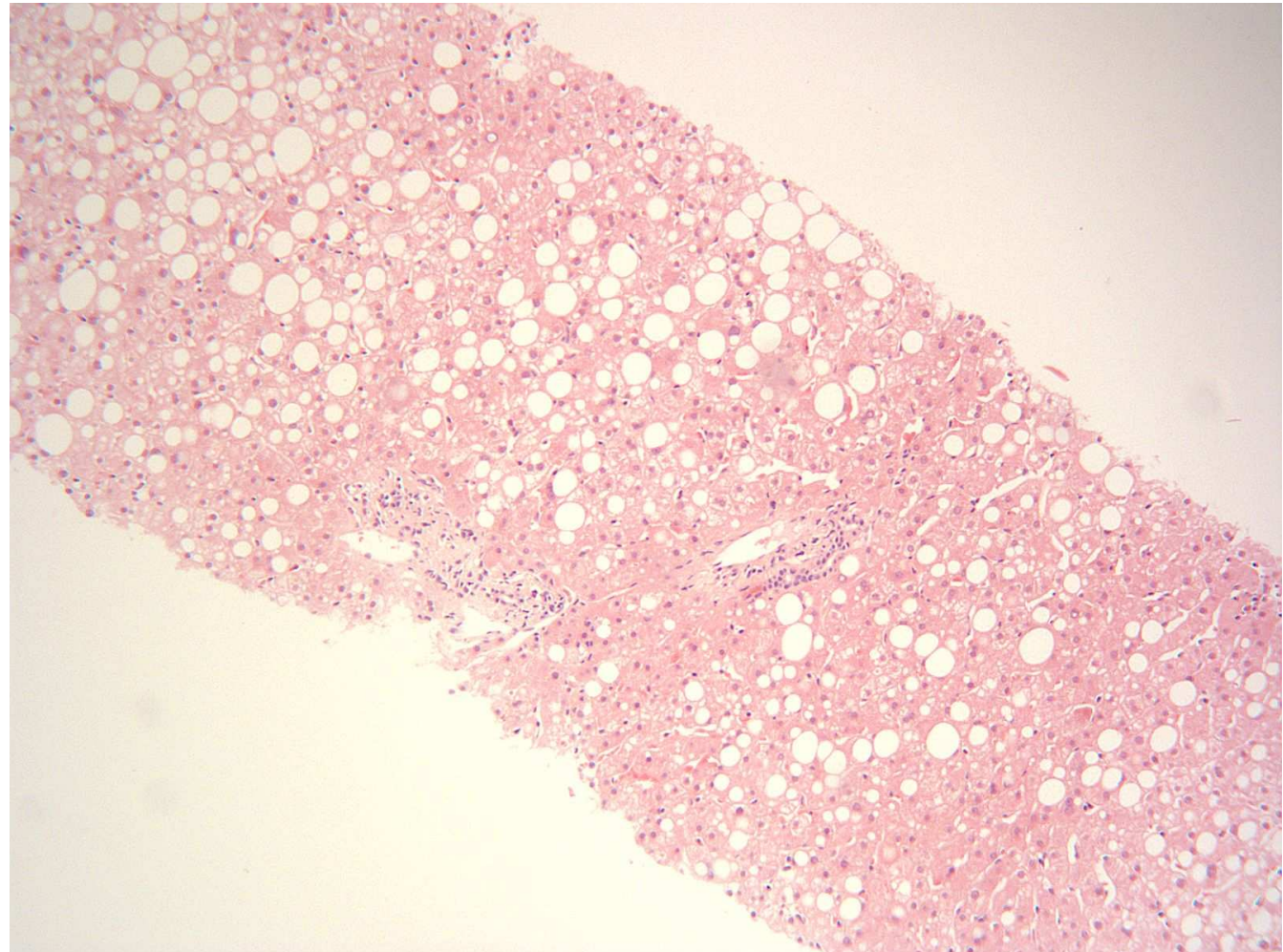
Treatment individually tailored in each patient

## For example:

Male, 33, chinese, ALT x3 upper limit of normal

HBsAg +ve, HBeAg +ve

HBV DNA  $>10^6$



# Questions to Hepatologists

- What to put in report?

Biopsy size – adequacy, ideally >10 portal tracts

short or narrow biopsies underestimate severity

Chronic viral hepatitis

Any other disease – relative contributions

i.e. is raised ALT due to the viral hepatitis

or something else?

Severity of fibrosis stage and necroinflammatory grade

Ishak score or words

- Who to discuss in CPC?

All hepatitis B

?All Hepatitis C or only if requested.