Hepatitis B:
How many of the 85,000 people living with undiagnosed chronic hepatitis B are attending your practice?

Tuesday 18 June 2019
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Postdoctoral Fellow, Doherty Institute Epidemiology Unit
Where is my control panel?
You have been placed on “mute” to optimise the learning experience for you and your peers.

Use the question box function to talk to us.
Conflict of interest

• No conflicts of interest to declare
Acknowledgement of Country

We wish to acknowledge the traditional custodians of the land. We acknowledge and respect their continuing culture and the contribution they have made to the life of this city and this region. We pay our respects to Elders past and present.
Learning Objectives

- Identify priority populations for hepatitis B testing in Australia
- Correctly order HBV diagnostic tests
- Interpret serology to determine a patient’s hepatitis B status
- Describe the intervention points throughout the natural history of HBV using the HBV decision making tool
- Explain the need for treatment and regular lifelong monitoring of patients with chronic hepatitis B
Overview

1. Epidemiology
2. Why worry?
3. Transmission and prevention
4. Testing and interpreting results
5. Hep B positive…. What now?
6. Monitoring and treatment
Polling Question 1
Is Hepatitis B really an issue?

How many people worldwide are living with Chronic Hepatitis B?

a. 1 million
b. 50 million
c. 150 million
d. 250 million
NOTE for RACGP - This is a question slide pls format as required

Answer = D
Cherie Bennett, 28/05/2019
Hep B is one of the world’s most common infectious diseases

It is the second most important known human carcinogen after tobacco.

250 MILLION PEOPLE WORLDWIDE ARE LIVING WITH CHRONIC HEP B (CHB)

EVERY 44 SECONDS, someone dies because of their hepatitis B infection. This equates to 715,000 deaths per year.

Geographic distribution of hepatitis B

Over half of all people on Earth live in an area with intermediate or high prevalence.

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CDA Foundation 2017, Schweitzer at al. 2015
Polling Question 2
Hepatitis B in our backyard

How many new hepatitis B infections are notified in Australia each year?

a. 250 – 500
b. 1000-1500
c. 3000-4000
d. 6000-70000
2

NOTE for RACGP - This is a question slide pls format as requiried

Answer = D
Cherie Bennett, 28/05/2019
Hepatitis B in Australia

- 234,000 estimated living with CHB
- 6,000 - 7,000 newly notified infections every year
- 1% prevalence overall; 4% prevalence in Aboriginal and Torres Strait Islander people
- 343 GPs accredited to prescribe treatment (s100)

Viral Hepatitis Mapping Report 2017; NNDSS 2018
People living with CHB in Australia, by priority population, 2017

Some of our closest neighbours, South and North-East Asia, make up 41% of these populations.
Key points: Epidemiology

- Hepatitis B is a worldwide issue
- The majority of people living with chronic hepatitis B in Australia are migrants from high prevalence areas, particularly Asia and the Pacific
- Aboriginal and Torres Strait Islander Australians are also a priority population with a high prevalence of chronic hepatitis B
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CHB and Liver Cancer

• CHB is the most common cause of hepatocellular carcinoma (HCC) worldwide
• Risk of developing HCC is 20 to 100 times higher in people living with CHB relative to those without infection
Early detection is key

If HCC is detected, **urgently** discuss with or refer to specialist

Carville et al 2018
Overview

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6. Monitoring and treatment and monitoring
Transmission of HBV infection

**Vertical/perinatal**
- HBeAg + / high viral load → active/passive vaccination less effective

**Horizontal**
- Skin, mucosal breaks; schoolchildren

**Sexually Acquired**
- Unprotected vaginal, anal or oral sex with a person who has hepatitis B

**Percutaneous**
- IDU, tattoos, acupuncture, body piercing; household inc. toothbrush, razors

**Blood Transfusion**
- Transfusion safety; surgery, dentistry, dialysis, finger pricks; alternative health care

Lee 1997, Margolis et al. 1991
Polling Question 3

What is the likelihood a child infected with hepatitis B will go on to develop chronic infection?

a. 10%

b. 25%

c. 50%

d. 95%
NOTE for RACGP - This is a question slide pls format as requird

Answer = D
Cherie Bennett, 28/05/2019
Transmission of HBV infection

High prevalence countries/groups
- Most transmission perinatal or through early childhood contact
- >95% progression to chronic infection

Low prevalence countries/groups
- Primarily adults in risk groups through parenteral/percutaneous and sexual transmission
- <5% progression to chronic infection

Australia
- Overall low prevalence
- However, certain groups have a higher prevalence – culturally and linguistically diverse people (CALD) and Aboriginal and Torres Strait Islander people
**Risk of HBV infection from exposure to body fluids**

<table>
<thead>
<tr>
<th>High Risk</th>
<th>Safe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>Urine</td>
</tr>
<tr>
<td>Serum</td>
<td>Faeces</td>
</tr>
<tr>
<td>Wound exudates</td>
<td>Sweat</td>
</tr>
<tr>
<td>Semen</td>
<td>Tears</td>
</tr>
<tr>
<td>Vaginal fluid</td>
<td>Breast milk</td>
</tr>
</tbody>
</table>

Note: Salivary transmission is very rare and is through human bite exposures etc. where blood is present. **Sharing food & drink is NOT a risk.**
Vaccination

• Access the Australian Immunisation Handbook online at https://immunisationhandbook.health.gov.au/

• Immunisation is provided **FREE** for certain groups by a number of State and Territory Governments, and can be ordered by GPs through your health department. Check www.hepbhelp.org.au for more info.

• People at particular risk (sexual contacts of people with CHB, health care workers) should have an immunity check after vaccination.

• Non-responders are recommended to receive further doses and serological testing.
Key points: Transmission and prevention

- Most people living with CHB in Australia acquired the infection at birth or in early childhood
- Most acute hepatitis B infections in Australia are due to sexual transmission or unsafe injecting drug use
- People from certain groups may be able to access free immunisation depending on state/territory
- GPs play a critical role in prevention (vaccination, promoting harm minimization strategies i.e. needle and syringe exchange)
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Why is testing so important?

Cascade of Care

- Living with Chronic Hepatitis B Infection: 233,947
- Diagnosed: 149,024 (63.7%)
- Undiagnosed: 84,923 (36.3%)
- Engaged in Care: 47,161 (20.2%)
- Not in Care: 186,786 (79.8%)
- Estimated to Need Treatment: 46,789 (20.0%)
- Receiving Treatment: 19,358 (8.3%)
- Not Receiving Treatment: 27,431 (11.7%)

GPs play a critical role. Unless people are tested/diagnosed the remaining steps cannot occur.
Clinical indicators for testing

Patients may present with the following:

- Abdominal pain
- Fever
- Joint pain
- Loss of appetite
- Nausea and vomiting
- Weakness and fatigue
- Dark urine
- Yellowing of skin and whites of the eyes

Quite generic symptoms for many conditions … hence being aware of priority populations for opportunistic screening critical
Priority populations for testing

Opportunistically test people at risk, particularly

• People born in intermediate and high prevalence countries

• Aboriginal and Torres Strait Islander people
Priority populations for testing

Other patients whose HBV status should be determined:

• Pregnant women
• People about to undergo immunosuppression
• Unvaccinated adults at increased risk of infection, including
  • Sexual/household contacts and family members of those with hep B
  • Men who have sex with men
  • People who inject drugs
  • Sex workers/people with multiple sexual partners
  • Haemodialysis patients
• People living with Hepatitis C or HIV infection
• People with clinical presentation of liver disease/elevated ALT or AFP of unknown aetiology
• Health professionals involved with exposure-prone procedures
• Members of the armed forces

RACGP  ashm  ASHM 2018
Case study - Chen

- Chen is a 28-year-old Chinese student
- Presents following a recent trip to China
- Attend the funeral of his father, who died ‘of a liver tumour’.
- He is attending your practice as he had an apparent upper respiratory tract infection while overseas.

Use the Decision-Making in HBV tool throughout this case study
Polling Question 4

Should you opportunistically test Chen for hepatitis B? Refer to the decision making tool.

1. Yes
2. No

STEP 1 Should I test for HBV?

Who to offer testing to?
Answer

Yes

Chen is from China (high prevalence of chronic hepatitis B infection)

His father died from a ‘liver tumor’
STEP 2 To determine hepatitis B status, order 3 tests

- Hepatitis B surface antigen (HBsAg)
- Hepatitis B core antibody (anti-HBc)
- Hepatitis B surface antibody (anti-HBs)

You may miss an infection if all three are not requested

Do not just order ‘hepatitis B serology’ – the pathology service may not test for all three markers.
Testing for at-risk Australians is covered by Medicare.

All three tests are rebatable simultaneously. Write ‘? Chronic hepatitis B’ or similar on the request slip.

Doing HBV serology in a patient from a high prevalence background does NOT fall foul of the MBS screening provisions.
Case study - Chen

Chen’s serology is as follows:

- HBsAg: positive
- anti-HBc: positive
- anti-HBs: negative

What does this mean?

STEP 3 Interpreting serology
Polling Question 5

What does Chen’s serology mean?

1. Chronic HBV infection
2. Immune due to vaccination
3. Susceptible to infection
4. Immune due to resolved infection
Answer

What does Chen’s serology mean?

1. Chronic HBV infection
**STEP 3 Interpreting serology**

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>anti-HBc</th>
<th>anti-HBs</th>
<th>Chronic HBV infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>positive</td>
<td>positive</td>
<td>negative</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>anti-HBc</th>
<th>IgM anti-HBc*</th>
<th>anti-HBs</th>
<th>acute HBV infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>positive</td>
<td>positive</td>
<td>positive</td>
<td>negative</td>
<td>* (high titre)</td>
</tr>
</tbody>
</table>

**CRITICAL** for clinicians to test and diagnose these patients
### STEP 3 Interpreting serology

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>anti-HBc</th>
<th>anti-HBs</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>negative</td>
<td>negative</td>
<td>negative</td>
<td>Susceptible to infection (vaccination should be recommended)</td>
</tr>
<tr>
<td>negative</td>
<td>positive</td>
<td>positive</td>
<td>Immune due to resolved infection</td>
</tr>
<tr>
<td>negative</td>
<td>negative</td>
<td>positive</td>
<td>Immune due to hepatitis B vaccination</td>
</tr>
<tr>
<td>negative</td>
<td>positive</td>
<td>negative</td>
<td>Various possibilities including: distant resolved infection, recovering from acute HBV, false positive, ‘occult’ HBV</td>
</tr>
</tbody>
</table>
Key points: Testing and interpreting results

- Opportunistically test patients from priority populations
- Order all three serological tests
- Write ‘? Chronic hepatitis B’ on the request slip
- Do not just order ‘hepatitis B serology’
Overview

1. Epidemiology
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Range of illness with hepatitis B

- **Acute hepatitis B**
  - Asymptomatic
  - Acute self-limited hepatitis
  - Severe or fulminant hepatitis B

- **Chronic hepatitis B**
  - Asymptomatic
  - Chronic hepatitis
  - Cirrhosis
  - Liver failure
  - Hepatocellular carcinoma

About 20% of people with CHB die because of related complications (cirrhosis/liver cancer).
Initial assessment of HBsAg+ patients

- History (family and psycho-social)
- Physical examination
- Hepatitis B e antigen status (HBeAg and anti-HBe)
- HBV DNA level
- LFT, FBC, INR and alfa fetoprotein (AFP)
- Liver ultrasound or fibroscan
Initial assessment of HBsAg+ patients

• In addition:
  – Test for HAV, HCV, HDV and HIV (check for co-infection)
  – Evaluate co-morbidities - alcohol, drug use, diabetes, fatty liver and other morbidities
  – Discuss transmission and prevention of BBVs
  – Screen household contacts and sexual partners for HBV

These assessments will determine the PHASE of the disease and therefore TREATMENT and/or MONITORING requirements
There is no such thing as a ‘healthy carrier’
Case study - Chen

The results of Chen’s initial assessment show:

- **HBeAg**: positive
- **Anti-HBe**: negative
- **HBV DNA**: 7 log10 IU/mL (10,000,000 IU/mL)
- **ALT**: 50 U/L
- 3 months later: **ALT**: 55 U/L

Which phase of disease is Chen currently in?
Polling Question 6

Which phase of disease is Chen currently in?

1. Immune tolerance
2. Immune clearance
3. Immune control
4. Immune escape
**Answer**

**Natural History of Chronic HBV: The 4 Phases and Relevance to Treatment Decisions**

- **HBV DNA**
- **ALT**
- **HBeAg**
- **Anti-HBe**

**Immune Tolerance**
- High HBV DNA, Normal LFTs, HBeAg positive
- Monitor every 6-12 months

**Immune Clearance**
- High HBV DNA, Abnormal LFTs, HBeAg positive
- At risk of progression to cirrhosis and HCC therefore should be referred for consideration of treatment

**Immune Control**
- Low HBV DNA, Normal LFTs, HBeAg neg, anti-HBe pos
- Monitor every 6-12 months

**Immune Escape**
- High HBV DNA, Abnormal LFTs, HBeAg neg, anti-HBe pos
- At risk of progression to cirrhosis and HCC therefore should be referred for consideration of treatment
Key points:
Hep B positive... what now?

- There is no such thing as a ‘healthy carrier’
- Chronic HBV is a dynamic disease - patients move between phases
- Patients must be regularly monitored to determine which phase they are in
Overview

1. Epidemiology
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Polling Question 7

Use the HBV Decision Making Tool to determine which phases are indicated for consideration of treatment

1. Immune tolerance
2. Immune clearance
3. Immune control
4. Immune escape
Answer

Immune clearance and immune escape
## Key messages: Monitoring and treatment

<table>
<thead>
<tr>
<th>MONITORING</th>
<th>TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>• LFTs every 6 months</td>
<td>• Patients in immune clearance and immune escape phases</td>
</tr>
<tr>
<td>• HBV DNA test every 12 months</td>
<td>• Anyone with cirrhosis with detectable HBV DNA</td>
</tr>
</tbody>
</table>

Determine:
• if and when the disease phase has changed,
• when treatment may be indicated
First line treatments: entecavir and tenofovir (s100)

Patients will take one pill a day indefinitely

Safe and well-tolerated

Associated with almost no resistance

Treatment is usually life-long
Benefits of treatment

- Normalisation of ALT – limit liver damage due to immune-mediated inflammation and fibrosis
- Sustained suppression of viral replication
- HBeAg seroconversion (10-20% per year)
- Reduce risk of progression to cirrhosis and liver cancer
- HBsAg seroconversion is very rare
GP Prescribing for CHB

- Accredited GPs can prescribe treatment
- Community pharmacists are able to dispense Hep B s100 medications
- 343 accredited GP Prescribers in Australia
- HBV prescriber locator map available on ASHM website
- To enquire about becoming an accredited prescriber, contact HBVPrescriber@ashm.org.au

REMINDER:
ANY GP CAN PRESCRIBE TREATMENT FOR HEPATITIS C
Polling Question 8

You established that Chen is in the Immune Clearance phase. Should he be considered for antiviral treatment?

1. Yes
2. No
Answer

Yes.

Chen is in the Immune Clearance phase, meaning he is at risk of progression to cirrhosis and hepatocellular carcinoma (HCC).

He should be considered for antiviral treatment.
Polling Question 9

Should Chen be regularly screened for HCC?

a. No, Asian men only need screening when 40yrs+
b. Yes, he has a family history of HCC
**Answer**

Yes.

Chen has a family history of HCC - his father died of a liver tumour.

He should undergo 6-monthly surveillance with ultrasound + AFP.
Key points: Treatment and monitoring

• All patients with CHB need to be monitored every 6-12 months
• Not all patients with CHB require antiviral therapy
• Antiviral therapy is targeted at patients in the Immune Clearance (2) and the Immune Escape (4) Phases
• Entecavir and tenofovir are the first line antiviral therapies
• Accredited GPs can prescribe antiviral treatment in community settings
• GPs are essential in ensuring at-risk patients with CHB undergo surveillance for HCC
Take home messages: role of the GP

Testing and diagnosis
- Opportunistically test people at risk
- Order HBsAg + anti-HBc + anti-HBs

Vaccination

Ongoing monitoring
- No such thing as a healthy carrier
- All patients need regular monitoring
- Some patients require regular liver cancer surveillance

Treatment
- Treatment can prevent cirrhosis and liver cancer
- Can be prescribed by accredited GPs
Recap: Learning Objectives

- Identify priority populations for hepatitis B testing in Australia
- Correctly order HBV diagnostic tests
- Interpret serology to determine a patient’s hepatitis B status
- Describe the intervention points throughout the natural history of HBV using the HBV decision making tool
- Explain the need for treatment and regular lifelong monitoring of patients with chronic hepatitis B
QUESTIONS?
**Resources for clinicians**


**HepBHelp** is an independent website which aims to assist GPs in the further investigation and management of patients diagnosed with chronic hepatitis B infection: [www.hepbhelp.org.au](http://www.hepbhelp.org.au)

**Hepatitis B Online Modules**


**Decision making in HBV** - This is a quick reference guide to assist GPs in evaluating Hepatitis B laboratory results, understanding the natural history of chronic Hepatitis B and making decisions regarding the management and treatment of patients with Hepatitis B. [www.ashm.org.au/resources](http://www.ashm.org.au/resources)
The National Hepatitis B Testing Policy - The testing policy provides advice on appropriate testing pathways using currently available technologies for all health professionals ordering and interpreting tests for hepatitis B.
www.testingportal.ashm.org.au/hbv

Hepatitis B and Primary Care Providers - This booklet explains the role of primary care providers in hepatitis B diagnosis and management.
www.ashm.org.au/resources

The Australian Immunisation Handbook - Provides clinical advice for health professionals on the safest and most effective use of vaccines in their practice.

GESA Chronic Hepatitis B (CHB) Clinical Guidelines and Updates:


RACGP: National Faculty of Aboriginal and Torres Strait Islander Health www.racgp.org.au/yourracgp/faculties/aboriginal/

B Seen, B Heard: Hepatitis B from our perspective – This DVD contains personal accounts from people living with chronic hepatitis B. It is hoped the stories related here will increase awareness and understanding of chronic hepatitis B, reinforce understanding of its management, and reduce stigma and discrimination. www.ashm.org.au/products/product/1976963408
Resources for patients

**Hepatitis Australia** - Hepatitis Australia is an independent, charitable, community-based membership organisation offering assistance to people affected by viral hepatitis. [https://www.hepatitisaustralia.com/](https://www.hepatitisaustralia.com/)  
*Hepatitis Information Line*: 1800 437 222

**Hepatitis B Story** - An educational tool designed to support health workers in a discussion about chronic hepatitis B with patients who have low health literacy levels. [https://www.svhm.org.au/health-professionals/specialist-clinics/g/gastroenterology/resources](https://www.svhm.org.au/health-professionals/specialist-clinics/g/gastroenterology/resources)