GLMS GP CME

November 2023

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Gastroenterologist

What are the risk factors for gastric cancer?

a) Chronic Helicobacter pylori infection

b) Obesity

c) Male gender

d) Use of proton pump inhibitor

e) Increasing age

f) Diabetes

g) Family history of gastric cancer

h) Pernicious anaemia

i) Smoking

j) Non European ethnicity

k) All the above

What are the risk factors for gastric cancer?

a) **Chronic Helicobacter pylori infection**

b) **Obesity** → Increased risk of cardia cancer but not non cardia cancer

c) **Male gender** → 1.3-3x higher in men **but doesn't apply for cases <40**

d) Use of proton pump inhibitor
- Conflicting evidence

e) **Increasing age**

Age >45 associated with higher odds for progression of premalignant lesions to gastric cancer

Banks et al. Gut 2019; 68(9): 1545-75

What are the risk factors for gastric cancer?

- In US & UK populations, white subjects have lower risk than
  - Asian subjects: 2.1 fold higher incidence
  - Black subjects: 1.7 fold higher incidence
  - Hispanic-Latino subjects: 1.7 fold higher incidence
- Among Asian people, Korean and Chinese subjects have highest risk of a premalignant gastric lesion
  - Korean: OR 7.39 (95% CI 7.06-7.73)
  - Chinese: OR 4.77 (95% 4.54 – 5.01)

Banks et al. Gut 2019; 68(9): 1545-75

f) Diabetes

g) **Family history of gastric cancer** → Risk is higher if age of onset <50

h) **Pernicious anaemia**

i) **Smoking** → 1.45-2x higher in smokers

j) **Non European ethnicity**

k) All the above

What are the risk factors for gastric cancer?

- Retrospective study of 133 new cases of GOJ & gastric cancer between 2003 & 2009 at Middlemore Hospital
- Pacific (37%), Maori (26%)
- Younger age at diagnosis for Maori (59.3 years) & Pacific (64.5 years) c.f. European (77.2 years)
- Higher % diffuse type gastric cancer in Maori (62%) & Pacific (51%) c.f. European (18%)

Biggar et al. NZMJ 2011; 124(1331): 39-44

f) Diabetes

g) Family history of gastric cancer

h) Pernicious anaemia

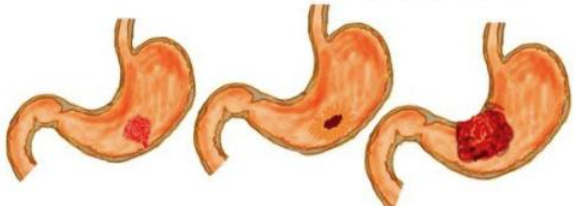
i) Smoking

j) Non European ethnicity

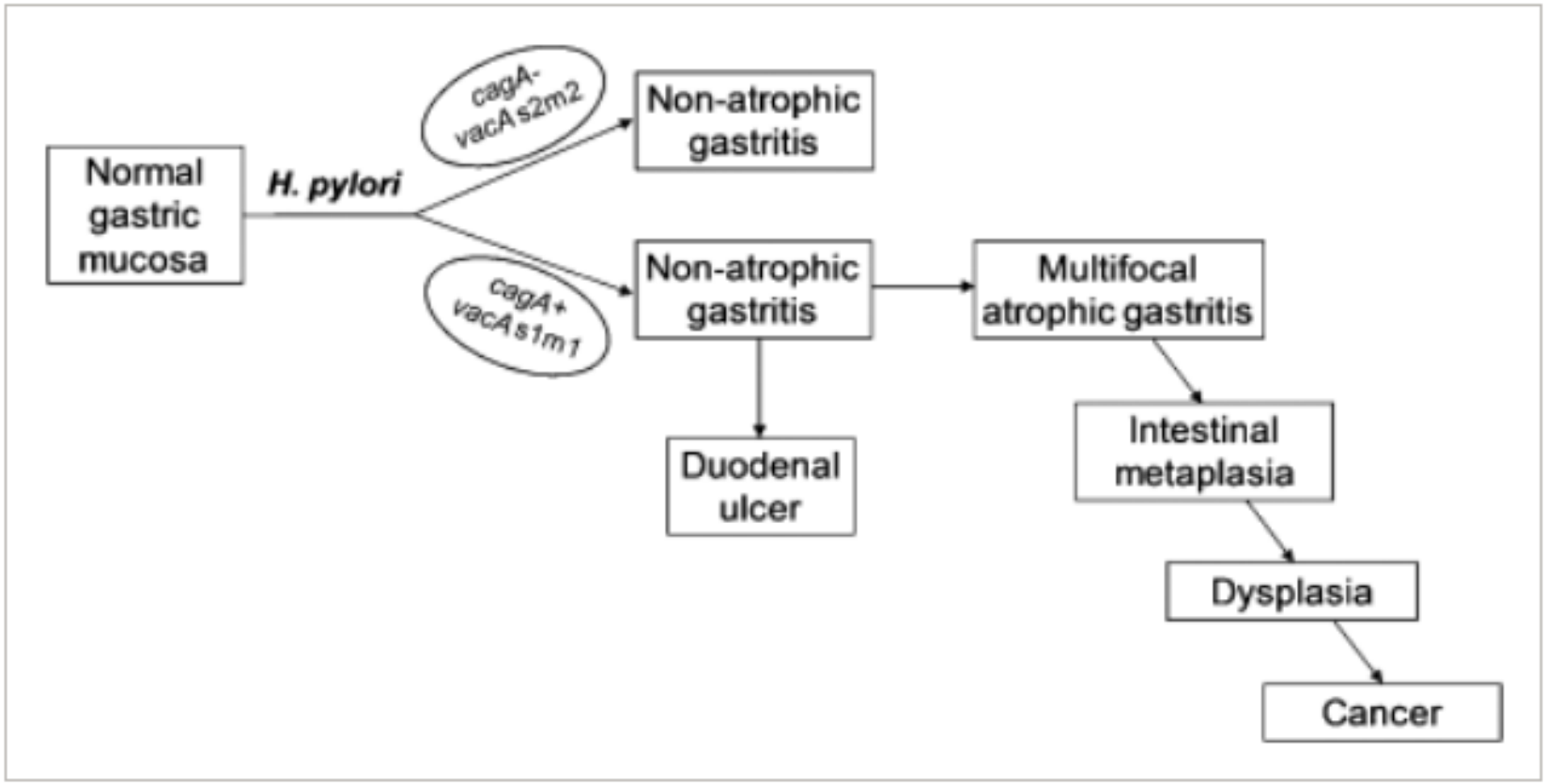
k) All the above

Gastric adenocarcinoma – Lauren classification

Intestinal type	Diffuse type
Environmental	Familial – loss of E-cadherin protein
Gastric atrophy, intestinal metaplasia	No identified precursor lesions
Increasing incidence with age	Can occur in younger individuals
M>F	F=M
Gland formation	Poorly differentiated
Bulky tumour (often exophytic or ulcerated)	Infiltrative tumours resulting in gastric wall stiffening (linitis plastica)



Correa cascade for intestinal type gastric cancer



Correa et al. J Dig Dis 2012; 13: 2-9

Case 1 – Ms HP

- 40 year old woman
- Dyspeptic symptoms
- Elevated H.pylori IgG

What is your go to H.pylori eradication therapy?

a) Omeprazole, Amoxicillin & Metronidazole

b) Omeprazole, Amoxicillin & Clarithromycin

c) Omeprazole, Metronidazole & Clarithromycin

d) None of the above

Case 1 – Ms HP

- 40 year old woman
- Dyspeptic symptoms
- Elevated H.pylori IgG
- Completed 14 day course of OAC
- H.pylori stool antigen 8 weeks later positive

What will you do next?

a) 14 day course of Omeprazole, Amoxicillin & Metronidazole

b) 14 day course of quadruple therapy

c) 14 day course of Omeprazole, Metronidazole & Clarithromycin

d) Refer for a gastroscopy for H.pylori culture

Case 1 – Ms HP

Previously failed 14 day course of Omeprazole, Amoxicillin and Clarithromycin

If you choose to start empirical quadruple therapy, what would be your treatment regime?

a) 14 day course of Omeprazole, Amoxicillin, Tetracycline and Gastrodenol

b) 14 day course of Omeprazole, Metronidazole, Tetracycline and Gastrodenol

c) 14 day course of Omeprazole, Clarithromycin, Tetracycline and Gastrodenol

d) None of the above

Case 1 – Ms HP

- 40 year old woman
- Dyspeptic symptoms
- Elevated H.pylori IgG
- Completed 14 day course of Omeprazole, Amoxicillin and Clarithromycin
- H.pylori stool antigen positive
- Treated with 14 day course of Omeprazole, Metronidazole and Clarithromycin
- Repeat H.pylori stool antigen positive

Case 1 – Ms HP

- Referred to Gastro => triaged directly for a gastroscopy
- Gastroscopy reported gastritis involving gastric fundus & gastric body
- Histology
  - Gastric body biopsies: mild active chronic Helicobacter associated gastritis
  - Gastric antral biopsies: moderate active chronic Helicobacter associated gastritis with focal intestinal metaplasia

Case 1 – Ms HP

SITE : Gastric Biopsy

CULTURE :

(1) Helicobacter pylori isolated

MINIMUM INHIBITORY CONCENTRATION

Organism : Helicobacter pylori

Antibiotic : Amoxicillin
MIC : 0.064 mg/l (Susceptible)

Antibiotic : Clarithromycin
MIC : 48.0 mg/l (Resistant)

Antibiotic : Tetracycline
MIC : 0.094 mg/l (Susceptible)

Antibiotic : Metronidazole
MIC : 12.0 mg/l (Resistant)

- Treated with 14 day course of

  Omeprazole 20mg bd

  Amoxicillin 1g bd

  Gastrodenol 120mg QID AND

  Tetracycline 500mg QID (need SA application)

Case 1 – Ms HP

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- Repeat H.pylori stool antigen positive

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c) 14 day course of Omeprazole, Clarithromycin, Tetracycline and Gastrodenol

d) None of the above

Helicobacter pylori resistance to drugs

- Clarithromycin “all or none”
  - Not overcome by increasing dose & duration
  - Should not be used if prevalence **>15-20%**
- Metronidazole “not all or none”
  - Overcome by increasing dose & duration
  - Should not be used if prevalence **>40%**
- Amoxicillin – rare in most regions
- Tetracycline – rare in most regions
- Bismuth – does not occur

Graham et al. Drugs 2008; 68: 725-736

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Observational Study > N Z Med J. 2013 Oct 18;126(1384):64-76.

Increasing primary antibiotic resistance and ethnic differences in eradication rates of Helicobacter pylori infection in New Zealand--a new look at an old enemy

	1999	2012
Clarithromycin resistance	7%	16.4%
Metronidazole resistance	32.7%	**49.3%**
Moxifloxacin resistance	N/A	9.5%

- Clarithromycin resistance prevalent among Maori, Pacific People & Orientals

Case 1 – Ms HP

- Histology
  - Gastric body biopsies: mild active chronic Helicobacter associated gastritis
  - Gastric antral biopsies: moderate active chronic Helicobacter associated gastritis with **focal intestinal metaplasia**

Does this patient need regular surveillance gastroscopies?

a) Yes

b) No

c) Depends on her family of gastric cancer

d) Unsure

Gastric intestinal metaplasia (GIM)

- Common finding on gastroscopy
  - Especially with current or past H.pylori infection
- Prevalence also increases with age, smoking & FHx of gastric cancer
- Extent of distribution appears to be of key importance
  - More extensive GIM (antral & body) correlates with higher gastric cancer risk

Table 3 The risk of cancer for patients with gastric atrophy and intestinal metaplasia

	5-Year incidence of gastric cancer (%)	Annual incidence (%)
All GA	1.9	0.1–0.5
Mild GA	0.7	
Severe GA	10	
All GIM		0.15–0.4 0.25
Antral GIM	5.3	
Antral and corpus GIM	9.8	
	Interval of 4–48 months	
Low-grade dysplasia	0–23	0.6
High-grade dysplasia	60–85	6

GA, gastric atrophy; GIM, gastric intestinal metaplasia.

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Gastric cancer risk in patients with premalignant gastric lesions: a nationwide cohort study in the Netherlands

- Annual incidence of gastric cancer
  - Atrophic gastritis 0.1%
  - Intestinal metaplasia 0.25%
  - Mild to moderate dysplasia 0.6%
  - Severe dysplasia 6%

- Risk factors for gastric cancer development
  - Increasing severity of gastric premalignant lesions
  - Increased age
  - Male gender

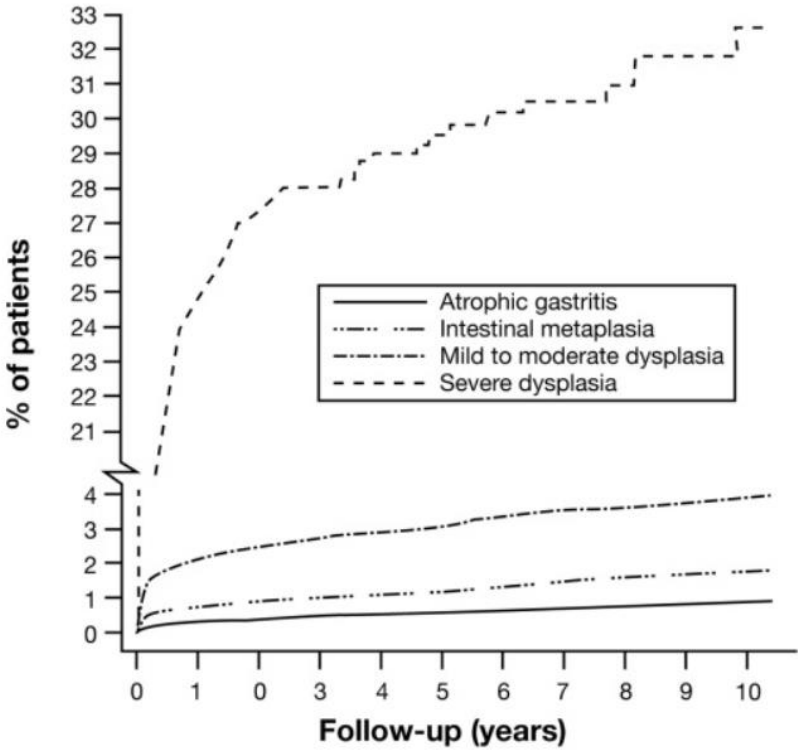

Figure 5 Progression rate of premalignant gastric lesions to gastric cancer in 92,250 patients with premalignant gastric lesions (90,780 censored patients).

De Vries et al. Gastroenterology 2008; 134(4): 945-52

Gastric cancer screening / surveillance?

- No formal screening program or surveillance recommendation in NZ

- British Society of Gastroenterology guidelines (Gut 2019; 68: 1545-75)
  - Consider screening for ≥50 with multiple RFs e.g. male, smoker, 1st degree relative with gastric Ca, pernicious anaemia

  - Atrophy or gastric intestinal metaplasia limited to gastric antrum => surveillance OGD every 3 years
    NOT recommended unless there are additional risk factors e.g. strong family history of gastric cancer or persistent H.pylori infection

  - Atrophy or intestinal metaplasia affecting gastric antrum & gastric body => surveillance OGD every 3 years

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Does this patient need regular surveillance gastroscopies?

a) Yes

b) No

c) Depends on her family of gastric cancer

d) Unsure

Case 2 – Mr HC

- 61 year old man
- PMHx: HTN, dyslipidaemia, gout
- Consumes 30ml whiskey Q2/12
- **ALT 280**, **GGT 86**, bilirubin, ALP & albumin normal
- HBsAg negative, anti-HBs 800 IU/L
- **HCV Ab reactive**, **HCV RNA 80000 IU/mL**
- Normal iron studies, ceruloplasmin & alpha-1 AT
- ANA negative

Parietal Cell Ab	POSITIVE A
Smooth Muscle Abs	Not detected
Mitochondrial Ab	Not detected

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What is your management?

a) Start 12 week course of Viekira Pak

b) Start 8 week course of Maviret

c) Start 12 week course of Maviret

d) Refer to Gastro clinic for review & further management

Case 2 – Mr HC

- Viekira Pak previously used to treat HCV genotypes 1a & 1b (now delisted)
- **Maviret available since Feb 2019**
  - Pan-genotypic so **HCV genotype testing no longer required**
  - **3 tablets once daily for 8 weeks**
- All HCV patients without evidence of cirrhosis can be treated in primary care

What is your management?

a) Start 12 week course of Viekira Pak

b) Start 8 week course of Maviret

c) Start 12 week course of Maviret

d) Refer to Gastro clinic for review & further management

- Previous failed treatment
- Evidence of cirrhosis
- Coinfection with HBV or HIV
- CrCl <30

Case 2 – Mr HC

Table 3: Examples of medicines which are contraindicated or should be used with caution in patients taking glecaprevir + pibrentasvir*:[5, 27]

Examples of medicines which are contraindicated	Examples of medicines that should be used with caution
▪ Simvastatin, atorvastatin ▪ Antiepileptic medicines, including phenytoin, primidone, phenobarbital, carbamazepine ▪ Combined oral contraceptives and ethinylestradiol + etonogestrel contraceptive ring ▪ Dabigatran ▪ Rifabutin and rifampicin ▪ Many medicines for the treatment of HIV ▪ Other medicines for the treatment of HCV	▪ Amiodarone ▪ Aripiprazole ▪ Carvedilol ▪ Cyclosporine ▪ Clozapine ▪ Colchicine ▪ Digoxin ▪ Domperidone ▪ Enalapril ▪ Erythromycin ▪ Ezetimibe ▪ Gemfibrozil ▪ Glibenclamide ▪ Ketoconazole ▪ Methotrexate ▪ Modafinil ▪ Opioid medicines: fentanyl, oxycodone ▪ Pravastatin ▪ Quetiapine ▪ Rivaroxaban ▪ Sulfasalazine ▪ Tacrolimus ▪ Theophylline ▪ Ticagrelor ▪ Verapamil ▪ Warfarin

What is your management?

a) Start 12 week course of Viekira Pak

b) Start 8 week course of Maviret

c) Start 12 week course of Maviret

d) Refer to Gastro clinic for review & further management

Case 2 – Mr HC

- 61 year old man
- **ALT 280**, **GGT 86**, bilirubin, ALP & albumin normal
- **HCV Ab reactive**, **HCV RNA 80000 IU/mL**
- Completed 8 weeks of Maviret
- Blood tests 4 weeks post treatment completion
  - **HCV RNA not detected**
  - LFTs normal

Do you need to check his HCV RNA again to confirm cure?

a) No, he is cured

b) Yes, check HCV RNA at 8 weeks post treatment completion to confirm HCV eradication

c) Yes, check HCV RNA at 12 weeks post treatment completion to confirm HCV eradication

d) Yes, check HCV RNA at 24 weeks post treatment completion to confirm HCV eradication

Case 2 – Mr HC

- Sustained virological response at 12 weeks post treatment (SVR12) **previously** recommended to confirm HCV eradication

- Gane et al. J Viral Hepat 2021; 28(11): 1635-1642
  - **>99% of pts treated with 8 weeks of Maviret will have sustained virological response at 4 weeks post treatment (SVR 4)**
  - **SVR 4 was highly predictive of SVR 12 in Maviret treated patients**
    - **PPV >99%**
  - 100% of those who failed to achieve SVR 4 did not achieve SVR 12

Do you need to check his HCV RNA again to confirm cure?

a) No as he is cured

b) Yes, check HCV RNA at 8 weeks post treatment completion to confirm HCV eradication

c) Yes, check HCV RNA at 12 weeks post treatment completion to confirm HCV eradication

d) Yes, check HCV RNA at 24 weeks post treatment completion to confirm HCV eradication

Case 2 – Mr HC

- Sustained virological response at 12 weeks

Do you need to check his HCV RNA again to confirm

No follow up required after successful treatment if

- Normal liver function tests
- No evidence of cirrhosis

HCV antibody will remain positive lifelong

Need ongoing Gastro follow up if

- Severe fibrosis or cirrhosis i.e. 6 monthly aFP and liver ultrasound

- 100% of those who failed to achieve SVR
  4 did not achieve SVR 12

Case 2 – Mr HC

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- **ALT 280**, **GGT 86**, bilirubin, ALP & albumin normal
- **HCV Ab reactive**, **HCV RNA 80000 IU/mL**
- Completed 8 weeks of Maviret
- Blood tests 4 weeks post treatment completion
  - **HCV RNA not detected**
  - LFTs normal

Does this patient need a Fibroscan?

a) Unsure

b) No

c) Yes, he likely has had HCV for many years given his age

d) Calculate APRI score

Case 2 – Mr HC

AST to Platelet Ratio Index (APRI)

Determines the likelihood of hepatic fibrosis and cirrhosis in patients with hepatitis C.

When to Use | Pearls/Pitfalls | Why Use

AST	46	U/L
AST upper limit of normal	45	U/L
Platelet count	175	$\times 10^3/\mu L$

0.6 points

Per Lin et al (2011), scores < 0.7 were not sensitive or specific enough to determine level of fibrosis or cirrhosis.

APRI score <1: cirrhosis is unlikely
APRI score ≥1: **may** have cirrhosis
=> fibroscan

Does this patient need a Fibroscan?

a) Unsure

b) No

c) Yes, he likely has had HCV for many years given his age

d) Calculate APRI score

Case 2 – Mr HC

Parietal Cell Ab	POSITIVE A
Smooth Muscle Abs	Not detected
Mitochondrial Ab	Not detected

Lab comment:
Parietal cell Abs are associated with pernicious anaemia. They are also found in 20-30% of patients with autoimmune endocrine disease such as thyroiditis & IDDM, and in 2-10% of the normal population

What would you do?

a) Nothing

b) Depends on patient's symptoms

c) Check intrinsic factor antibodies & vitamin B12

d) Refer for a gastroscopy

Pernicious anaemia – serology testing

- Parietal cell antibodies
  - High sensitivity (85-90%)
  - **Low specificity => high number of false positives**
- Intrinsic factor antibodies
  - Low sensitivity (~60%)
  - **Very specific => virtually diagnostic for pernicious anaemia**
  - Absence does not rule out pernicious anaemia

	Intrinsic factor antibody (IFA) ⊖ Negative	**Intrinsic factor antibody (IFA) ⊕ Postive**
Parietal cell antibody (PCA) ⊖ Negative	Pernicious anaemia unlikely	Immunological evidence of pernicious anaemia
Parietal cell antibody (PCA) ⊕ Positive	◦ Not diagnostic ◦ PCA positive in 85–90% of patients with pernicious anaemia ◦ Negative IFA does not exclude pernicious anaemia (only present in 50% or less)	Immunological evidence of pernicious anaemia

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Case 3 – Mr HB

- 59 year old man with elevated BMI
- HBV (e-antigen negative) diagnosed 8 years ago when he tried to donate blood
- Asymptomatic
- Drinks 3 alcoholic drinks twice a month
- ALT 58, otherwise LFTs normal

What will you do?

a) Advised patient to lose weight to treat empirically for fatty liver

b) Refer to the Hepatitis Foundation for 6 monthly blood test monitoring

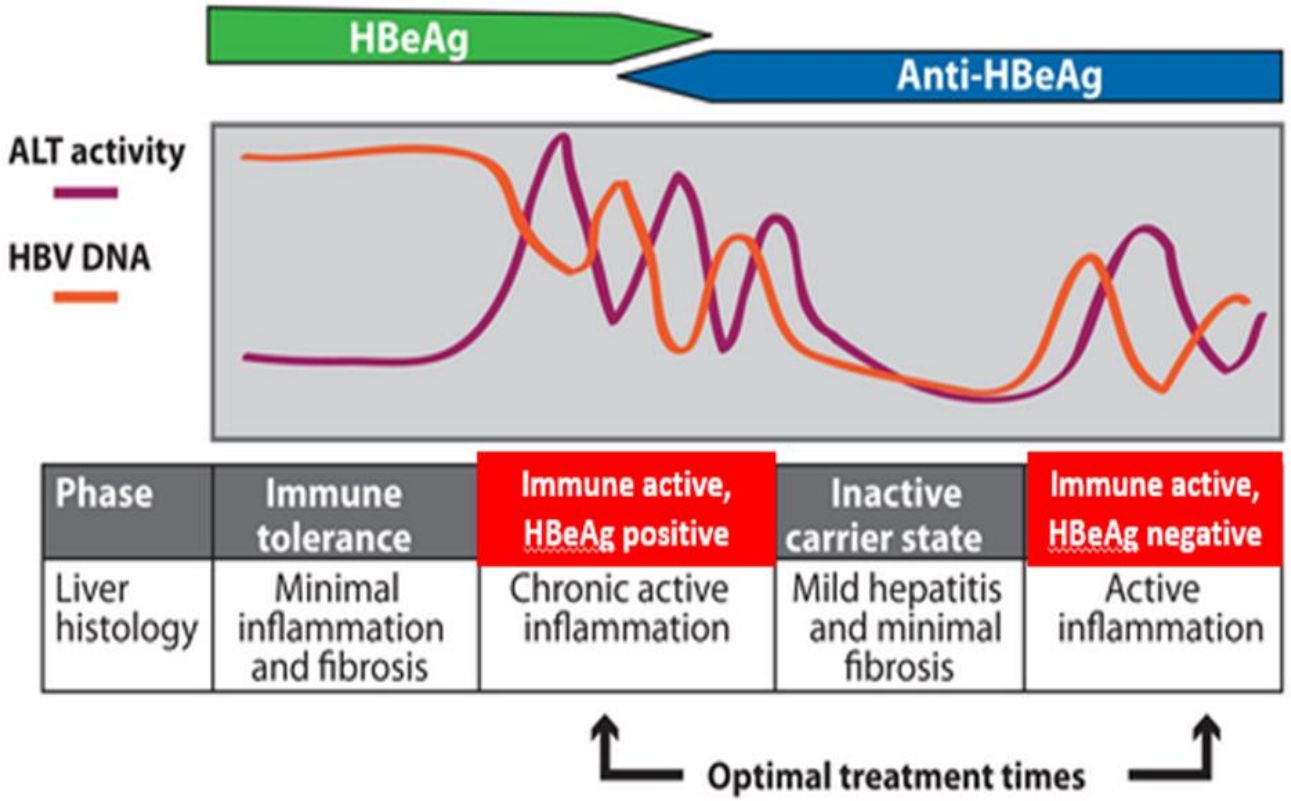
c) Check HBV DNA +/- liver screen

d) Refer to the Gastro clinic for review

Case 3 – Mr HB

- 59 year old Indian man with elevated BMI
- HBV (e-antigen negative) diagnosed 8 years ago when he tried to donate blood
- Asymptomatic
- ALT 58, otherwise LFTs normal
- **HBV DNA 7170000 IU/mL**

What phase of HBV is this patient in?



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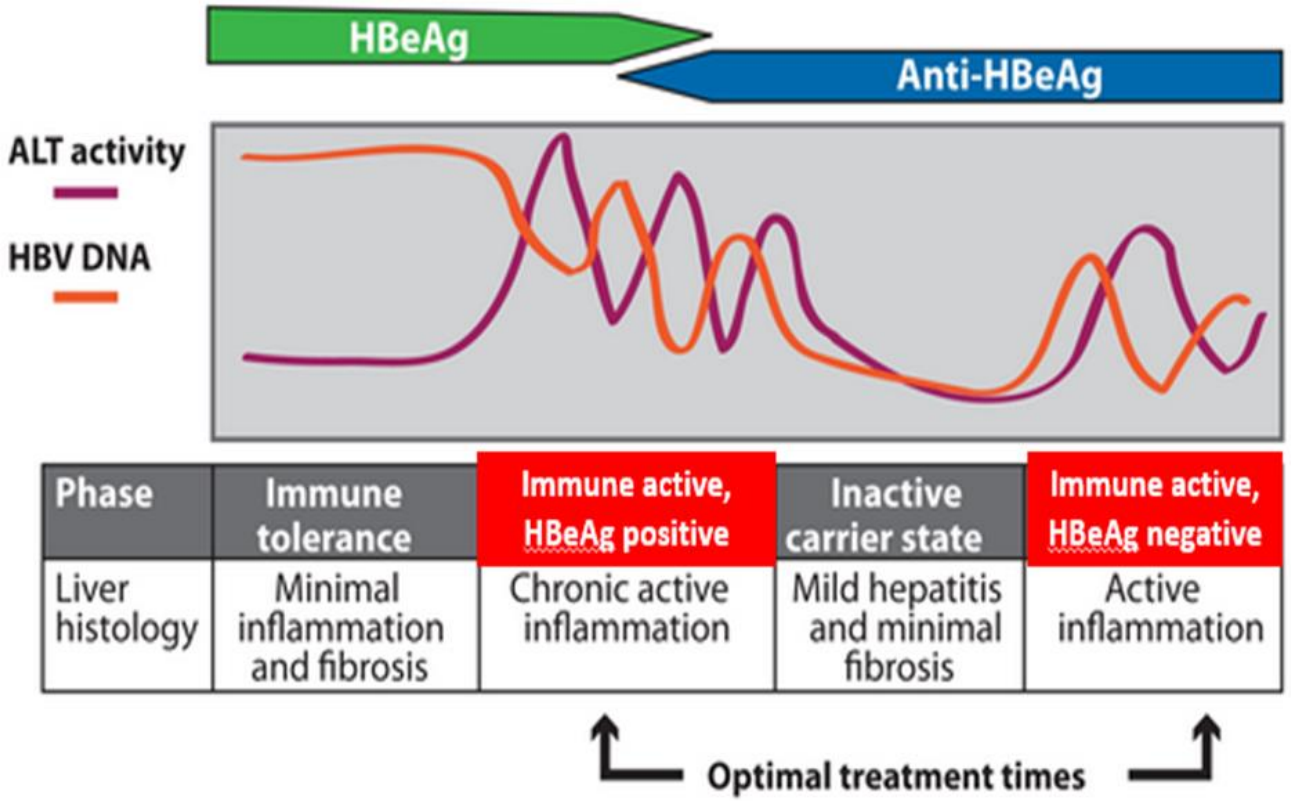
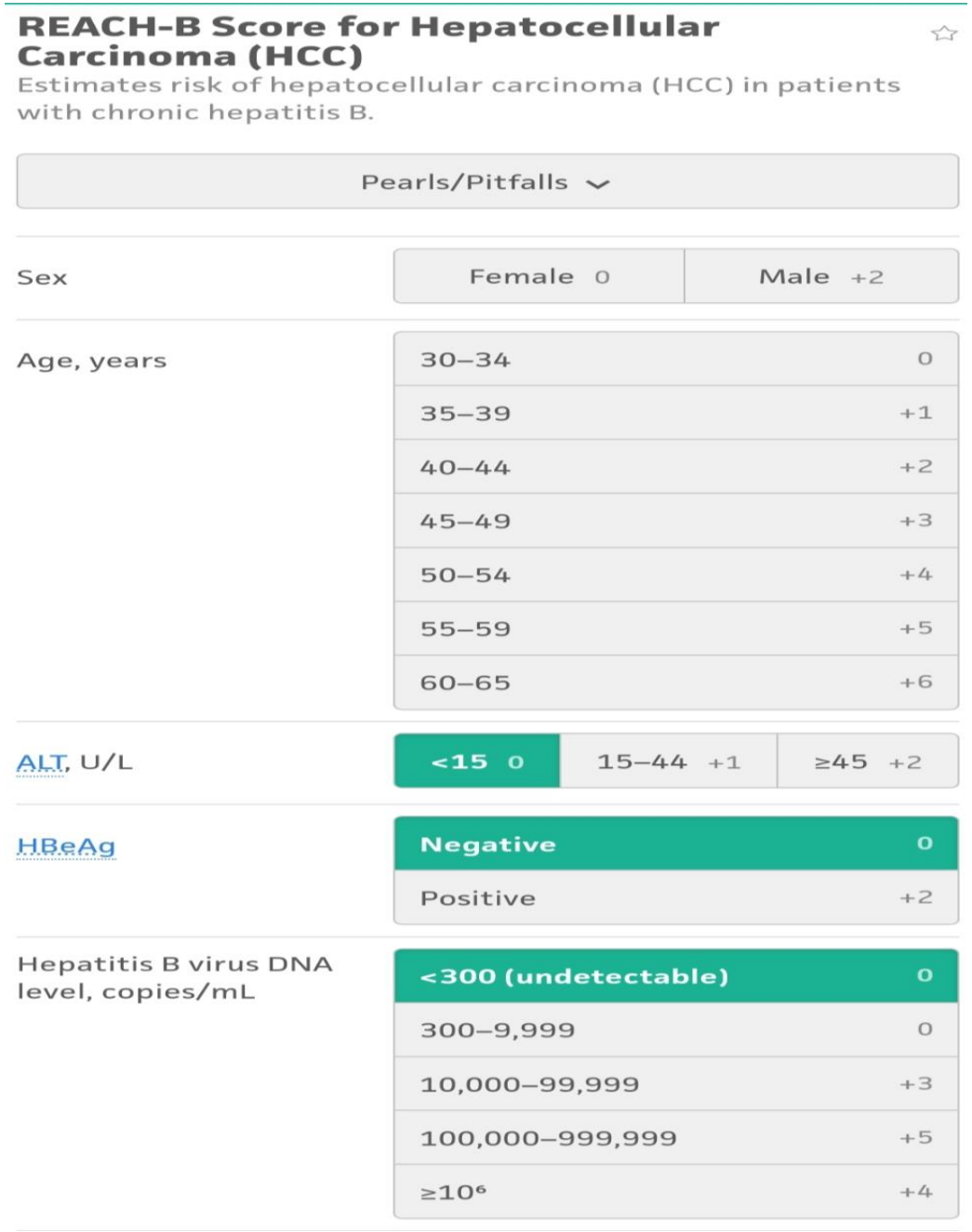
Does this patient need antiviral therapy?



REACH B score

- Developed to estimate the HCC risk of HBV patients at 3, 5 and 10 years



REACH-B Score for Hepatocellular Carcinoma (HCC)

Estimates risk of hepatocellular carcinoma (HCC) in patients with chronic hepatitis B.

Pearls/Pitfalls

Sex	Female 0	Male +2
Age, years	30–34	0
	35–39	+1
	40–44	+2
	45–49	+3
	50–54	+4
	55–59	+5
	60–65	+6
ALT, U/L	<15 0	15–44 +1 / ≥45 +2
HBeAg	Negative	0
	Positive	+2
Hepatitis B virus DNA level, copies/mL	<300 (undetectable)	0
	300–9,999	0
	10,000–99,999	+3
	100,000–999,999	+5
	≥10^6	+4

Case 3 – Mr HB

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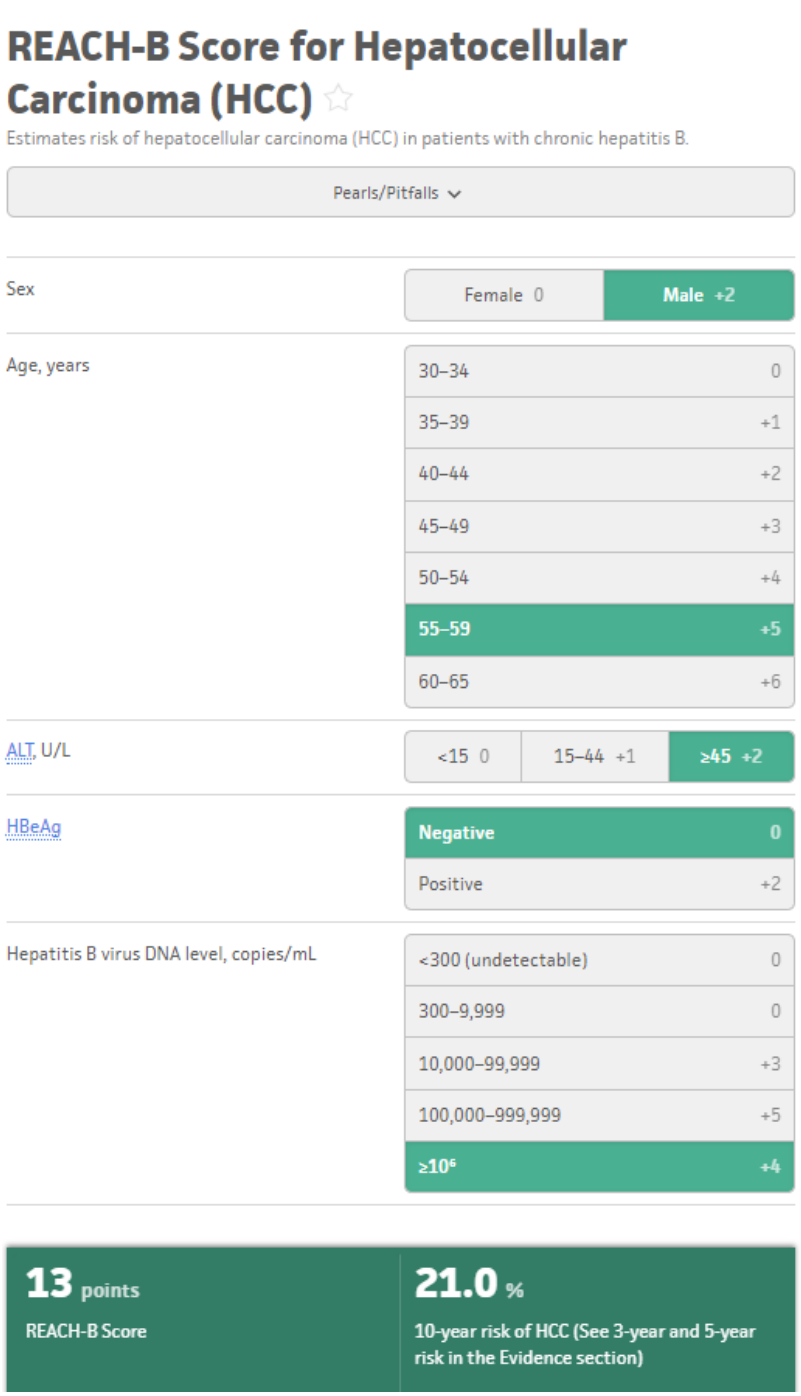

Case 3 -

- 59 year old
  elevated BI
- HBV (e-ant
  diagnosed
  tried to do
- Asymptom
- ALT 58, oth
- **HBV DNA 7**

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Pearls/Pitfalls

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Age, years	30–34 0	35–39 +1	40–44 +2
	45–49 +3	50–54 +4	**55–59 +5**
	60–65 +6		
ALT, U/L	<15 0	15–44 +1	**≥45 +2**
HBeAg	**Negative 0**	Positive +2	
Hepatitis B virus DNA level, copies/mL	<300 (undetectable) 0	**300–9,999 0**	10,000–99,999 +3
	100,000–999,999 +5	≥10⁶ +4	

9 points
REACH-B Score

3.2 %
10-year risk of HCC (See 3-year and 5-year risk in the Evidence section)

Antiviral therapy

REACH-B Score for Hepatocellular Carcinoma (HCC)

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Pearls/Pitfalls

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	45–49 +3	50–54 +4	**55–59 +5**
	60–65 +6		
ALT, U/L	<15 0	15–44 +1	**≥45 +2**
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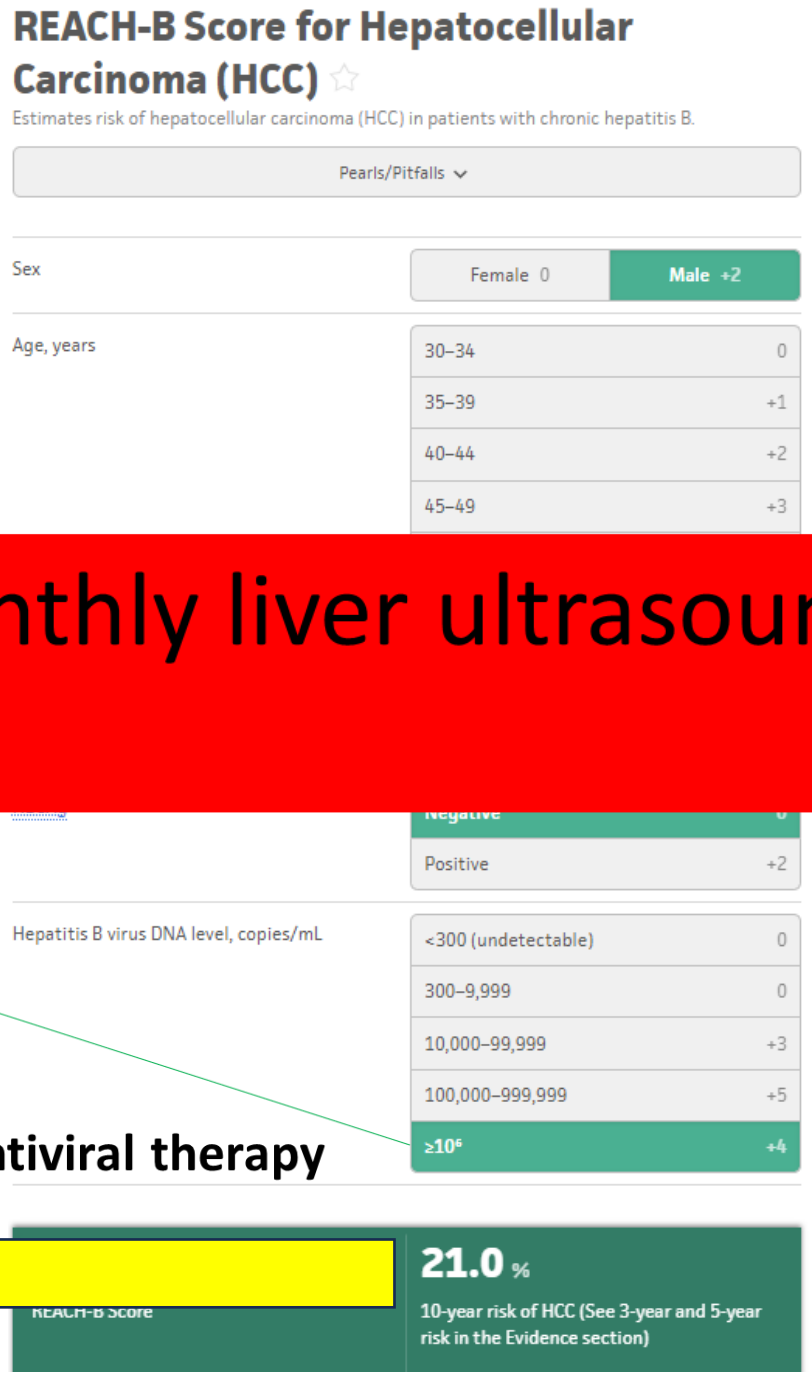
	100,000–999,999 +5	**≥10⁶ +4**	

REACH-B Score

21.0 %
10-year risk of HCC (See 3-year and 5-year risk in the Evidence section)

Case 3 -

- 59 year old
  elevated Bl
- **This patient will need 6 monthly liver ultrasound as HCC surveillance**
- Asymptom
- ALT 58, oth
- **HBV DNA 7**



Antiviral therapy

Case 3 – Mr HB

- 59 year old Indian man with elevated BMI
- HBV (e-antigen negative) diagnosed 8 years ago when he tried to donate blood
- Asymptomatic
- ALT 58, otherwise LFTs normal
- **HBV DNA 7170000 IU/mL**

Referred to Gastro clinic for review in May 2023

- 4 months later (i.e. September 2023)
  - Asymptomatic
  - **ALT 279, GGT 184**, otherwise LFTs normal
  - **HBV DNA 1060000 IU/mL**
  - **Alpha fetoprotein 132**
- Seen in Gastro clinic in mid October 2023 => started on Entecavir

Questions?