Gastrointestinal and Hepatology Cases

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GLMS CME 4 2019

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Outline

- Case 1 - LFTs
- Case 2 - Hepatitis
- Case 3 – Abdominal Pain and Diarrhoea
- Case 4 – PR Bleeding
- Case 5 - Biliary

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Case 1 Abnormal Liver Function Tests

- 60F
- Background of Metabolic Syndrome
  - IHD
  - T2DM
  - Hypertension
  - Dyslipididaemia
  - BMI 30

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Case 2 – Abnormal LFTs Work up?

- Liver screen
  - Viral Hepatitis (HBV, HBV, HCV (consider delta), HEV (acute presentation), EBV and CMV)
  - Auto-immune screen (ANA, AMA, LKM, SLA, Tissue Autoantibodies, Coeliac Ab, Globulins)
  - Rare causes (Ceruloplasmin, Alpha-1 antitrypsin)
  - Ferritin
  - INR
  - Albumin
- Ultrasound a good first step
- Role of Fibroscan?

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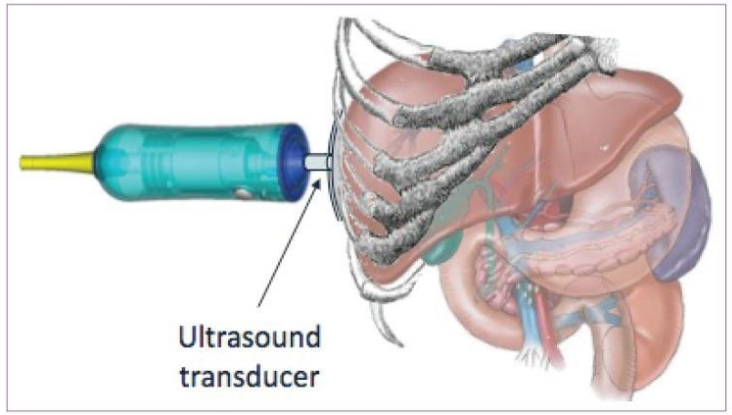
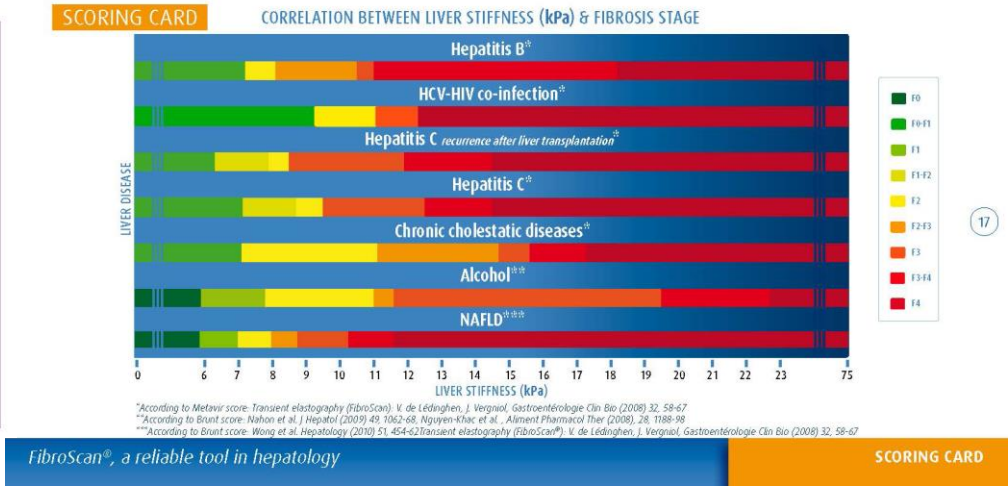
Fibroscan





- $355
- Covered by all insurance companies except Southern Cross

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Case 1 – Abnormal LFTs

- Work up - If persistent or worsening
  - Liver screen
  - Ultrasound
  - Consider Fibroscan
- Other features to watch out for
  - Is there pain? – Biliary (Stones, Dyskinesia), Other GI causes (Gastroscopy), Ultrasound, MRCP
  - Other features eg Low platelets, Low WBC, Low Albumin
  - Clinical feature of advanced liver disease

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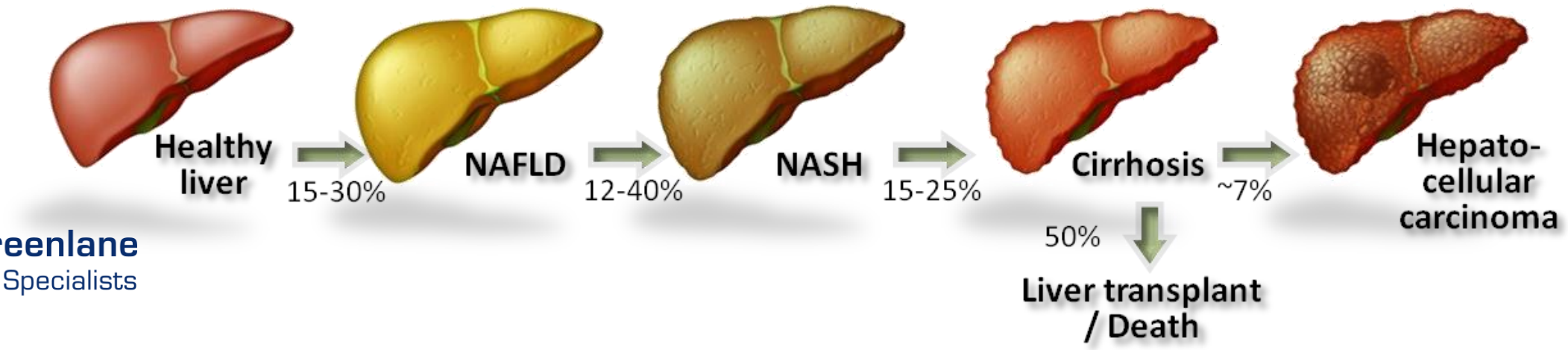
Case 1a – Non Alcoholic Fatty Liver Disease

- Most common liver problem
- Raised GGT, ALP, ferritin
- Diabetes
- Hypertension
- Genetic component in Asians

- No good pharmacotherapy at the moment
- Diet and exercise
- Bariatric endoscopy or Surgery



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When to refer to a specialist

- Pain with normal Ultrasound scan
- Assess fibrosis (risk stratify)
- Rule out other causes (ALT >100)
- Evidence of cirrhosis or portal hypertension

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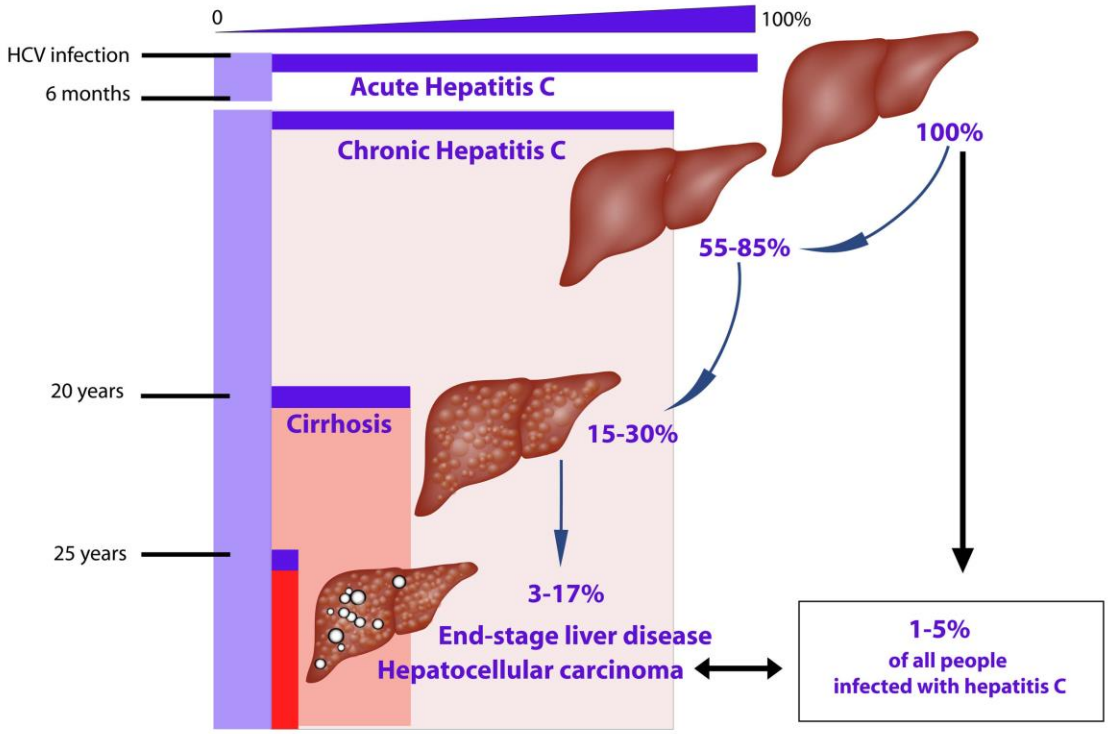
Case 2 – Chronic Hepatitis C



- 50000 New Zealanders
- 85% Chronic Infection
- 1/3 cirrhosis
- Up to 20% with end stage liver disease
- Genotype used to be important
  - Determines treatment success

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Case 2 HCV

- 45M Truck Driver
- No fixed abode
- Previous IVDU last used 12 months ago
- Admitted with abdominal pain and deranged LFTs
- CT shows nodular liver and pancreatic cystic lesion
- INR normal, Albumin normal, Platelets normal
- How should we manage him?

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Looking at hepatitis C in New Zealand
(estimated numbers)

An estimated
50,000 PEOPLE
have hepatitis C
in New Zealand

20,000 APPROX
have been diagnosed with
hepatitis C

11,000 APPROX
could have a diagnosis of
hepatitis C - genotype 1, and can
access funded treatment with
Viekira Pak through their GP in
the community right now

Just over
2,000 PEOPLE
with genotype 1 have had
funded treatment

Which means
9,000
people haven't accessed
funded treatment yet

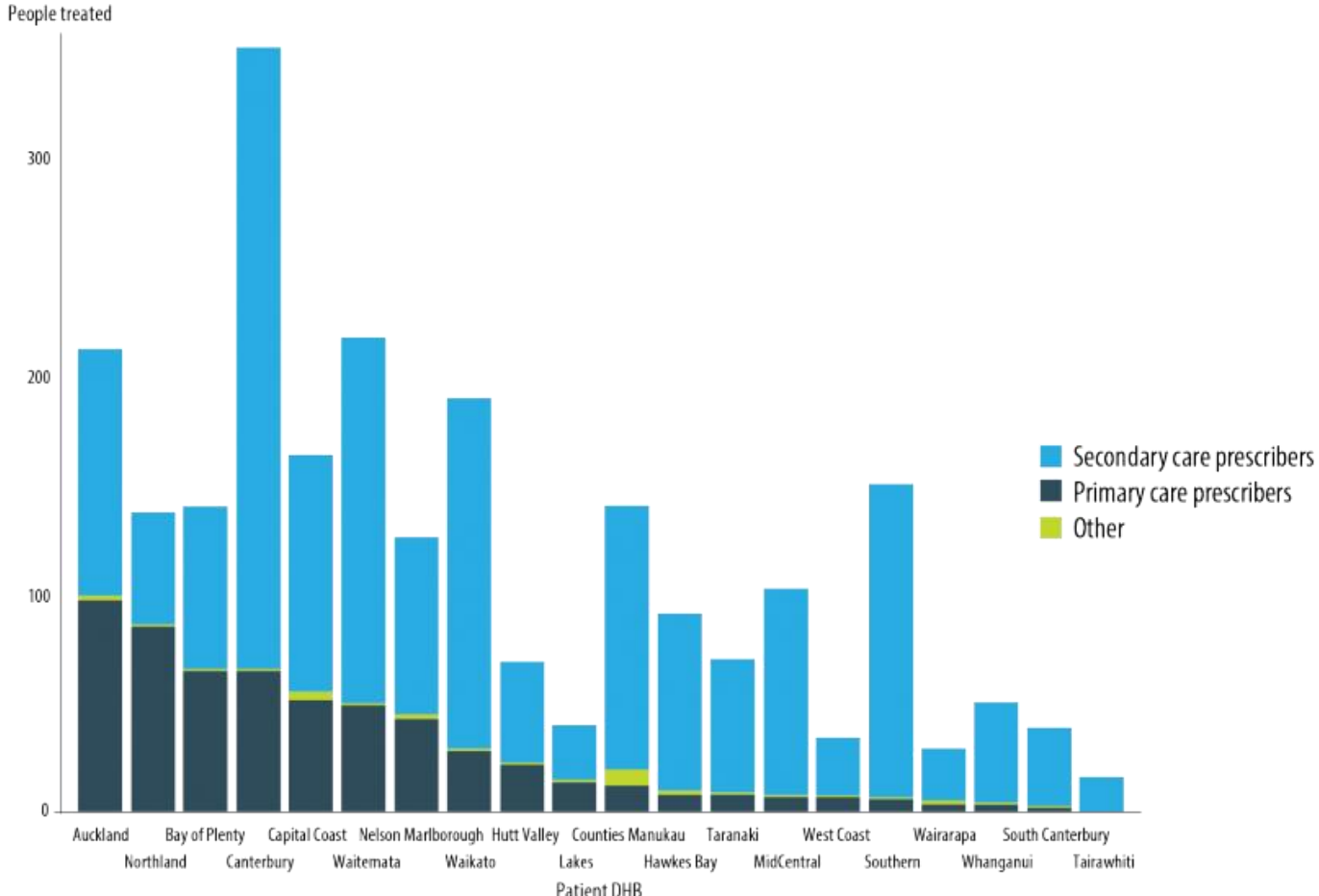

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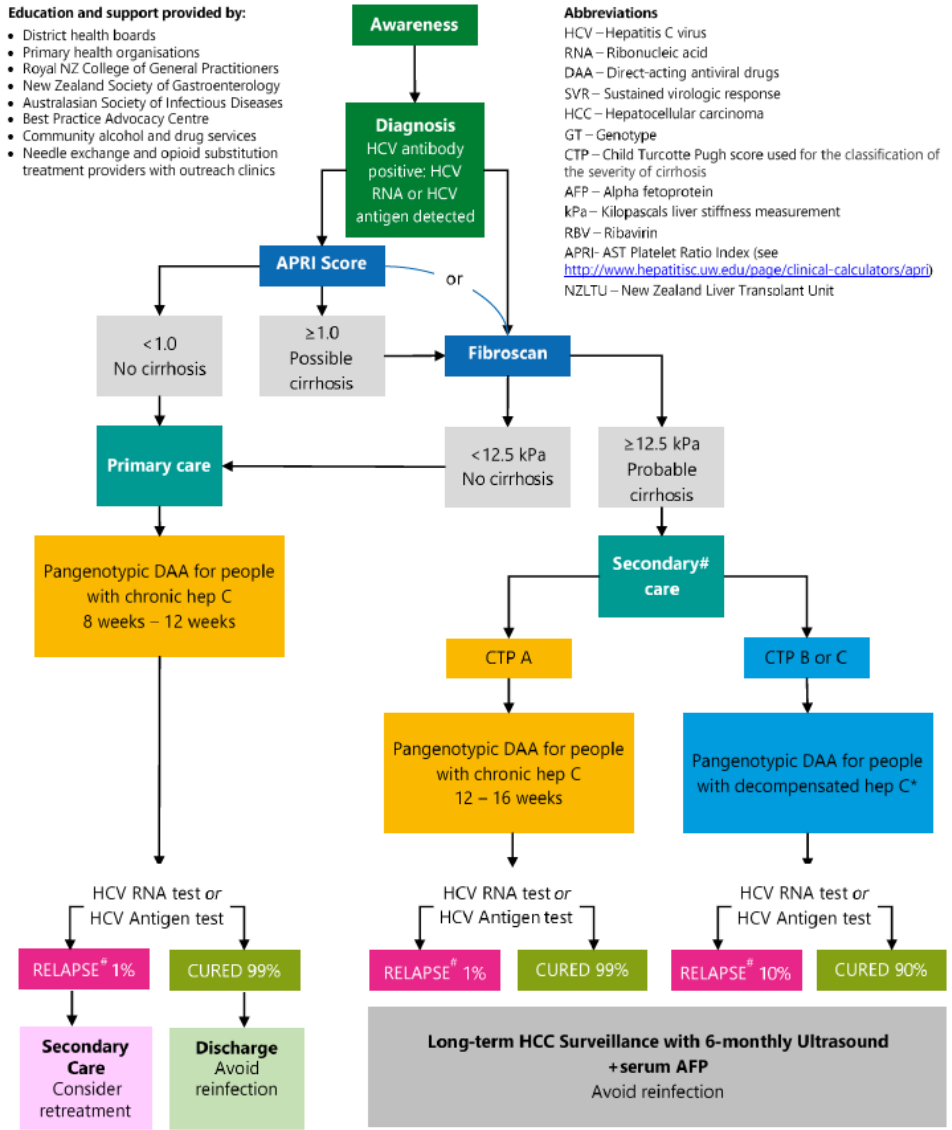
Figure one: Clinical pathway for hepatitis C based on integrated primary and secondary services



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Maviret

- Pangenotypic
- Compensated Cirrhotic and Non cirrhotic

MAVIRET will be funded in the community and DHB hospitals without restrictions for all compensated patients infected with HCV regardless of genotype, including those with compensated cirrhosis and those with HIV infection. It will replace VIEKIRA PAK in GT 1 patients.

1. Treatment naïve non cirrhotic patients infected with HCV GT 1-6 will receive 3 tablets once daily for 8 weeks
2. Treatment naïve cirrhotic patients infected with HCV GT 1-6 will receive 3 tablets once daily for 12 weeks
3. Interferon-experienced non cirrhotic patients infected with HCV GT 1, 2, 4, 5, or 6 will receive 3 tablets once daily for 8 weeks
4. Interferon-experienced cirrhotic patients infected with HCV GT 1, 2, 4, 5, or 6 will receive 3 tablets once daily for 12 weeks
5. Interferon-experienced non cirrhotic patients infected with HCV GT 3 will receive 3 tablets once daily for 16 weeks
6. Interferon-experienced cirrhotic patients infected with HCV GT 3 will receive 3 tablets once daily for 16 weeks.

DOSING GUIDE[1]

Recommended MAVIRET treatment duration for patients without prior treatment for hepatitis C

GENOTYPE	NO CIRRHOSIS	CIRRHOSIS‡
GT 1–6	8 weeks	12 weeks

Recommended MAVIRET treatment duration for patients who have previously failed prior therapy*

*peg-IFN + ribavirin +/- sofosbuvir, or sofosbuvir + ribavirin, or any of these in combination with a protease inhibitor.[1]

GENOTYPE	NO CIRRHOSIS	CIRRHOSIS‡
GT 1, 2, 4–6 NS5A-INHIBITOR NAÏVE	8 weeks	12 weeks
GT 1, 2, 4–6 NS5A-INHIBITOR EXPERIENCED*	16 weeks	16 weeks
GT 3 ANY PREVIOUS EXPERIENCE	16 weeks	16 weeks

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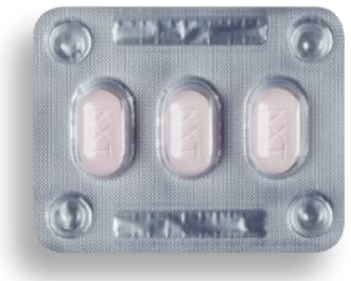
Formulation & Packaging

- Co-formulated, film-coated tablet of glecaprevir (100mg) and pibrentasvir (40mg)
- **Recommended oral dose is 3 tablets taken once daily with food**
- Tablets should be taken whole and not chewed, crushed or broken



Daily blister sheet

Weekly carton

Monthly carton (28 Days)

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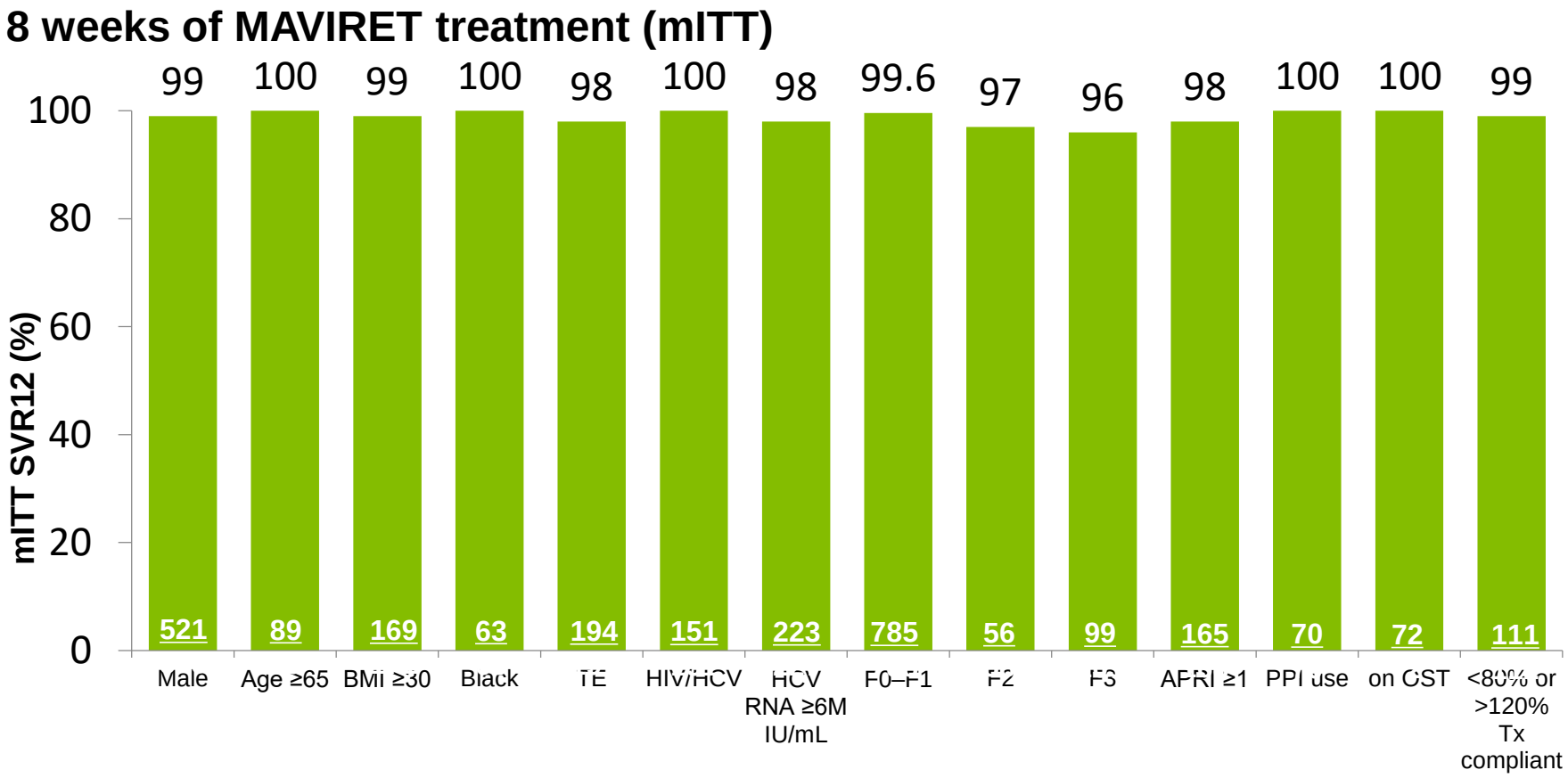
MAVIRET Data Sheet. Available at www.medsafe.govt.nz

Integrated Subgroup Analysis of Treatment-naive Non-cirrhotic Patients with HCV GT 1–6



High SVR12 was achieved irrespective of baseline patient and viral characteristics

APRI=aspartate aminotransferase to platelet ratio. BMI=body mass index. GT=genotype. HCV=hepatitis C virus. HIV=human immunodeficiency virus. mITT=modified ITT (excludes patients with non virologic failure). OST=opioid substitution therapy. pegIFN=peginterferon. PPI=proton pump inhibitor. RBV=ribavirin. RNA=ribonucleic acid. SVR=sustained virologic response. SVR12=HCV RNA below the lower limit of detection at 12 weeks post end-of-treatment. TE=treatment experienced. <80% or >120% compliance measured by pill count with adherence defined as taking between ≥80% and ≤120% of the assigned pills at treatment visits at week 4 and week 8.

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MAVIRET Data Sheet. Available at www.medsafe.govt.nz
Puoti M et al. J Hepatol 2018; doi: 10.1016/j.hep.2018.03.007

Summary

- MAVIRET is indicated for adult patients with HCV genotypes 1-6 with or without compensated cirrhosis (Child-Pugh A)
    - includes patients with HCV/HIV-1 co-infection, any stage of renal impairment (including those on dialysis), and HCV/HBV co-infection
- Dosing is 3 tablets taken orally, once daily; there is no dose adjustment for MAVIRET itself
- In phase 2 and 3 clinical studies, the adverse events observed in ≥5% of approximately 2,300 patients were headache, fatigue, and nausea
- Many drug interactions are not clinically relevant, or can be managed by monitoring and /or dose adjustment. Others are contraindicated, and should be stopped or switched to alternatives

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Harvoni

- For Decompensated Liver Disease
- Managed in secondary care

From 1 July 2016 until 12 June 2017, access to HARVONI was restricted to patients with decompensated cirrhosis with a Model for End-Stage Liver Disease (MELD) score of 15 or greater patients who were pre or post liver transplant and patients with cryoglobulinaemia. On 12 June 2017, the MELD threshold for patients with decompensated cirrhosis to access HARVONI was lowered from 15 to 12 in order to further widen access for this special population and increase salvage from death or transplantation. In December 2017, the criteria were widened further to include any patient who has decompensated cirrhosis (Child-Pugh class B or C) regardless of MELD score. To date, 161 patients with decompensated cirrhosis have been treated with HARVONI±RBV.

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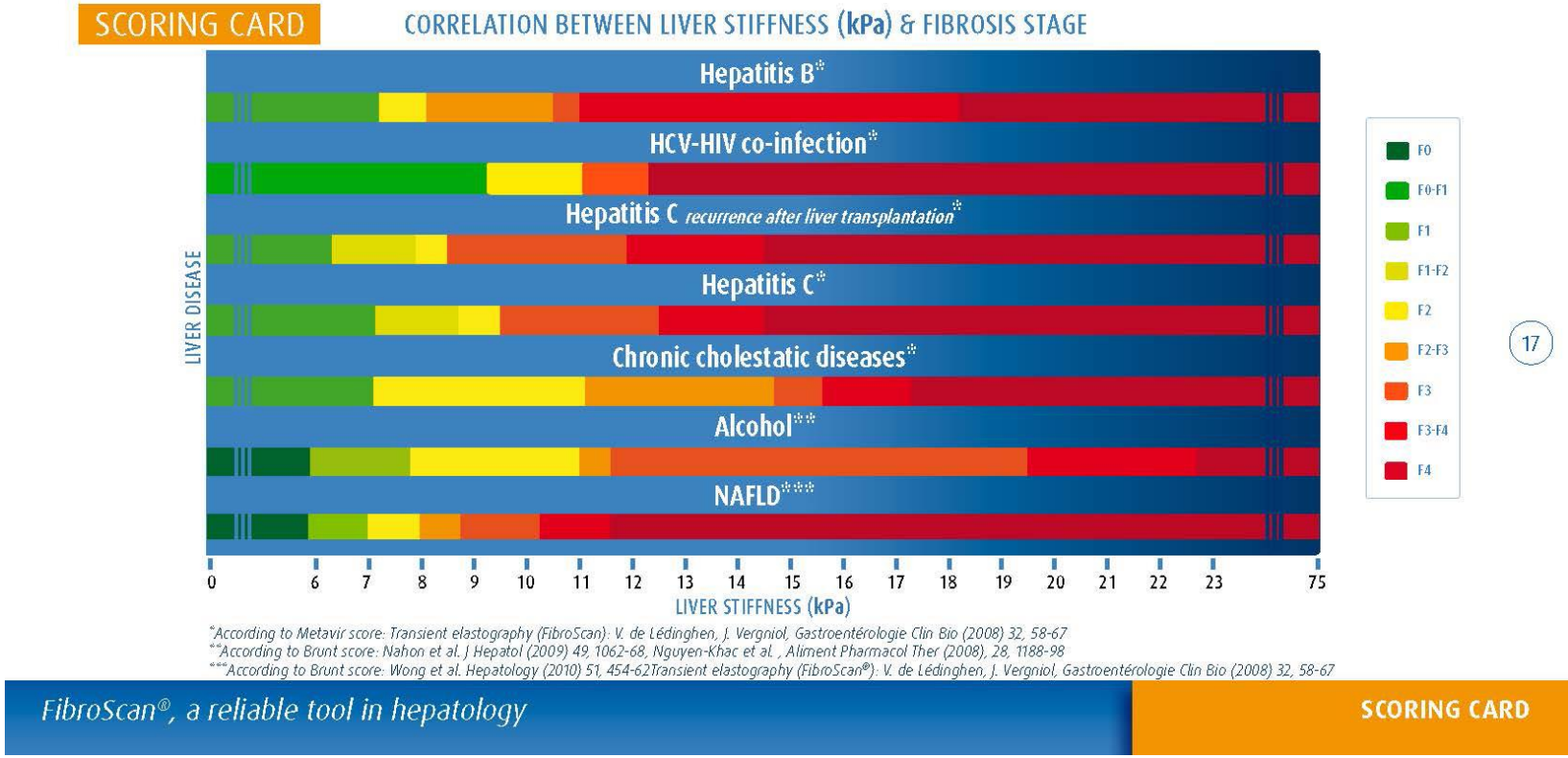
Fibroscan



- $350
- Covered by all insurance companies except Southern Cross

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Treatment

- Normal LSM
- Treated with 8 weeks of Maviret
- Dispensed at certain pharmacies

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Risk of HCC by Aetiology

- **Hepatitis B** – Annual incidence 0.5-1.0% per year in non cirrhotics, 2.5% per year in cirrhotics. RR 100
- **Hepatitis C** – Population based study n=12000, presence of Anti-HCV Ab – 20 fold increased risk of HCC. HCC may occur in HCV with bridging fibrosis. Cirrhosis 2%-8% per annum
- **Alcoholic Cirrhosis** – True incidence unknown
- **Metabolic Syndrome** – insulin resistance, Hypertension, Dyslipidaemia, obesity -> NASH. Incidence unknown. Probably around 5-10% have cirrhosis, 1-5% HCC
- **Biliary Cirrhosis** – Similar to Hepatitis C
- **Chronic Liver Injury** – Cirrhosis, 5 year risk of HCC ranges between 5-10% depending on ae/ology (highest for HCV) and stage of cirrhosis
- **Haemochromatosis** – RR 20

Case 3 Upper and Lower GI Symptoms with Change in Bowel Habit > 6 weeks

- 60 year old male
- BMI 30
- Weight loss 5kg
- Diarrhoea with upper and lower abdominal discomfort 2 months
- A) What is the diagnosis?
- B) How should we work him up?
- C) What is his risk of GI malignancy?

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Case 3 - Upper and Lower GI Symptoms with Change in Bowel Habit > 6 weeks

- Coeliac Disease
- Inflammatory Bowel Disease
- Microscopic Colitis
- Pancreatic Insufficiency
- Pelvic floor dysfunction
- Post Cholecystectomy Diarrhoea/ Bile Acid Diarrhoea
- Over-flow diarrheoa
- Malignancy

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Case 3 Upper and Lower GI Symptoms with Change in Bowel Habit > 6 weeks – Work up

Bloods

- Bloods
  - FBC
  - UEC
  - Ferritin
  - CRP
  - Coeliac antibodies
  - LFTs

Other

- Faecal Testing
  - M/C/S
  - Faecal Calprotectin
  - Faecal Steatorcrit

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Case 3- Upper and Lower GI Symptoms with Change in Bowel Habit > 6 weeks

Gastroscopy

- Biopsies
- Disaccharidases

Colonoscopy

- Biopsies

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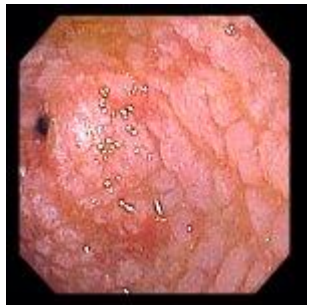
Endoscopic Findings

Gastroscopy

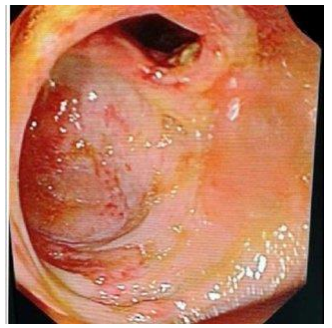
- Pangastritis
- Nodular antrum and body

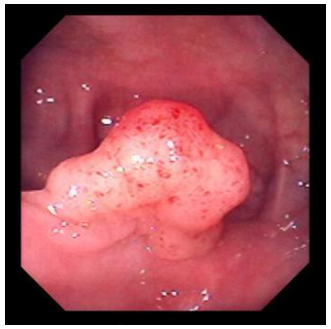


- What is the diagnosis?

Colonoscopy

- Colonic Polyps x 4 (5-10mm)
- Terminal ileal and Caecal Ulceration





- What are the Diagnoses?

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Histological Findings

Gastroscopy

- Pangastritis

- Biopsies
  - Intestinal Metaplasia with Helicobacter pylori

Colonoscopy

- Colonic Polyps x 4 (5-10mm)
- Terminal ileal and Caecal Ulceration

- Biopsies
  - Tubular Adenoma with low grade dysplasia
  - Yersinia Enterocolytica, TB PCR and cultures negative

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Endoscopic Surveillance

Gastroscopy

- Helicobacter pylori plus diffuse Intestinal Metaplasia – 12-18 months – localized 3 years

Colonoscopy

- Colonic Polyps – 10mm or > 3 adnenoma -> 3 years otherwise 5 years. Proximal Hyperplastic polyp – serrated – 3-5 years

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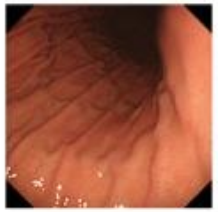
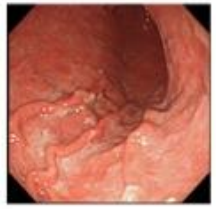
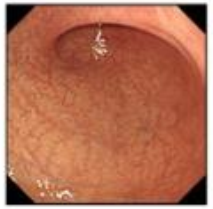
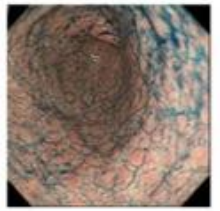
Helicobacter pylori

- Common in Asia (50-80%)
- < 10% Pakeha
- 30-50% South East Asia
- Indications for Treatment
  - Cancer Prevention
    - High risk individual (smokers, Family history, atrophic gastritis, intestinal metaplasia)
  - Symptoms
    - Dyspepsia
  - Peptic Ulcer Disease
  - MALT lymphoma
- Triple Therapy (OAC, OMC)
- Second line – Denol (Bismuth subcitrate 120mg QID or 240mg BD), Tetracycline 250mg QID or 500mg BD, PPI 400mg BD, Metronidazle 500mg BD or TDS 14 days

HP-related chronic gastritis stage	Group A HP(-), PG(-)	Group B HP(+), PG(-)	Group C HP(+), PG(+)	Group D HP(-), PG(+)
	Non-HP infection	Established HP infection	Extensive CAG	Metaplastic gastritis
				
Annual incidence of gastric cancer	0%	Approximately 0.1%	Approximately 0.25%	Approximately 1%
Prevention of gastric cancer		HP eradication	NSAIDs	

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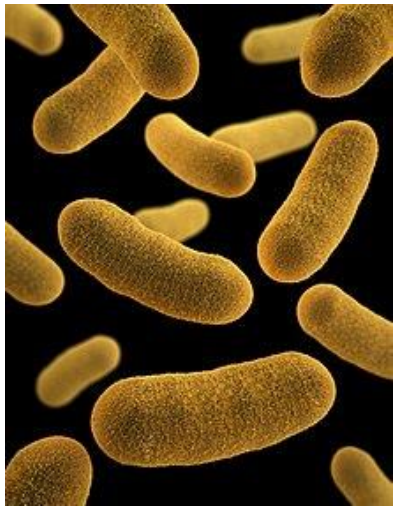
Yersinia Entercolytica



- Most self limiting
- Notifiable Disease
- Children < 5 years : Diarrhoeal illness
- Adults : Pain, Mesenteric adenitis, Bacteraemia (Immunocompromised)
- Reservoir: Y Enteroclytica - Pigs (Chinese people like pork!) Y pseudotuberculosis – Avian and Mammals (deer)
- Incubation 3-7 days (less than 10) Faecal shedding 2-3 weeks but can be months
- Ingestion
- Survives freezing and grows well in a refrigerator (4 degrees)
- Rx Ciprofloxacin for persistent symptoms

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Risk of Gastric Cancer

- NZ: 2015 - 383 cases (235M, 148 F) Incidence Rate = 5.3/100000 • 70% from developing countries, 50% from Eastern Asia
- **Increased Risk** • Chronic Atrophic Gastritis • Intestinal Metaplasia • Gastric Adenoma • FHx of Gastric Cancer • Li Fraumeni syndrome • Blood type A • Low fruit and vegetable consumption • Salted, smoked or poorly preserved foods • Cigarette smoking (60% higher risk in male smokers, 20% female smokers) • Radiation exposure • Helicobacter pylori – antrum and body adenocarcinoma and lymphoma
- **Reduced Risk** - Smoking cessation RR 1.2 vs 1.6 • Hp eradication RR 0.65 (1.7%->1.1%), incidence reduced by 39% (not mortality)

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Risk of Bowel Cancer

- Increasing age - 90% >50 years
- FDR < 55y – Doubles risk
- Personal Hx CRC, High risk adenomas
- Ovarian Cancer increases the risk
- Others:
  - IBD > 8 years
  - Genetics (<5% - FAP, HNPC)
  - Alcohol >45g per day)RR 1.41
  - Cigarette smoking RR 1.18
  - Obesity BMI >29 RR 1.45
  - Personal and FHx CRC

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Bowel Cancer Screening

- North, West, South and East Auckland
- 60-74 y – Happy Birthday !
- + FIT -> Colonoscopy -> 70% Polyps -> 7% (9% CMDHB) Cancer
- 50-55% uptake
- Encourage your patients

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Case 4 – PR Bleeding

- 29 year old male
- PR bleeding intermittently for 3 months
- Outlet type
- Normal Bowel Habit

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Case 4 – PR bleeding

- PR Bleeding
  - Acute infection
  - IBD
  - Haemorrhoids
  - Fissues
  - Bowel Cancer
  - Ischaemic Colitis

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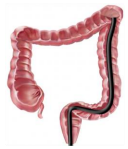
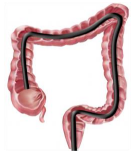
Case 4 – PR bleeding



Flexible Sigmoidoscopy +/- banding

- Age < 45 y
- No Change in Bowel Habit
- No other Risk factors



Colonoscopy

- Age > 45 y
- Change in Bowel Habit
- Smoker
- High Alcohol intake
- Overweight (Fatty liver increases polyps
- Unexplained Iron Deficiency

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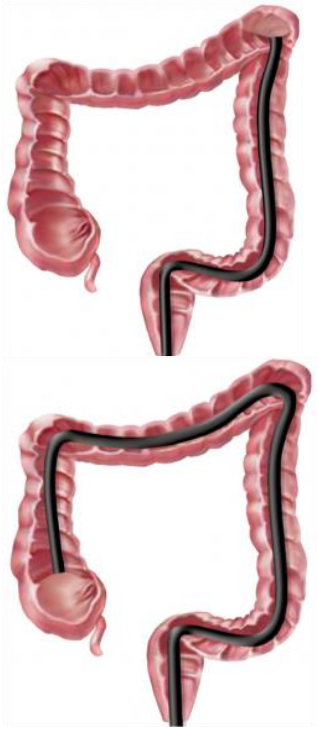
Case 4 – PR bleeding Clinic – “One stop shop”

- **<u>Colorectal Surgeon – Ms Sze Lin Peng</u>**
  - Patient Consultation
  - Flexible Sigmoidoscopy or Colonoscopy +/- banding
  - Single Visit
  - If IBD-> refer to Gastroenterologist
  - If External Haemorrhoids -> Surgery
  - If Fissures -> Medical therapy



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AUCKLAND COLORECTAL CENTRE

Case 5 – Upper Abdominal Pain

- 40F
- 12 months of Right Upper Quadrant Pain
- LFTs fluctuate – ALP and GGT and ALT up and down
- USS Normal
- Background
  - SLE
  - Not on Methotrexate

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Case 5- Upper Abdominal Pain

- Normal Liver Screen
- Bloods normal
- Normal Physical Examination
- Where to from here?

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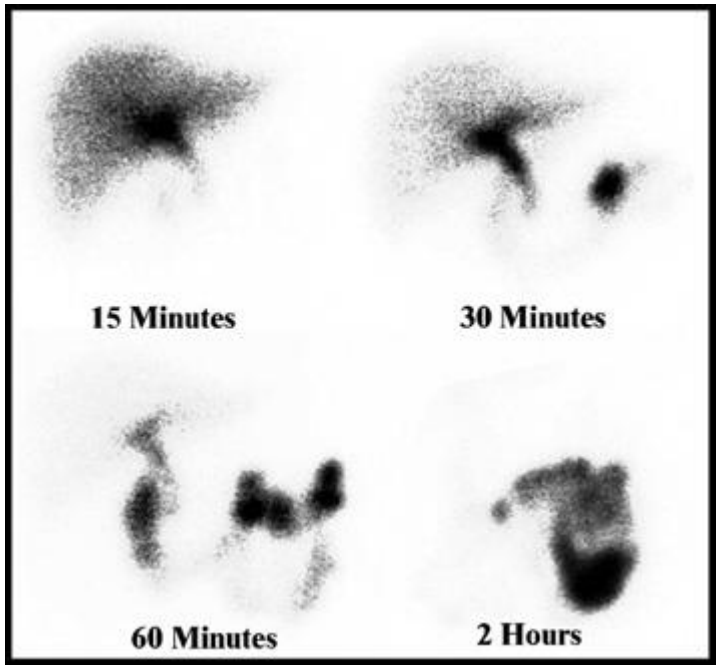
Case 5 – Upper Abdominal Pain

MRCP

- Normal Liver
- Normal Bile duct
- No Gallbladder sludge
- No features of Chronic Pancreatitis

HIDA scan

- Impression: The impaired gallbladder contraction and reduced ejection fraction In response to the fatty meal are consistent with gallbladder dysfunction / dyskinesia. Delayed hepatobiliary-tosmall intestinal flow is in keeping with generalised biliary dyskinesia.



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Case 5 – Upper Abdominal Pain

- **<u>Upper GI Surgeon– Mr Andrew MacCormick</u>**
  - Patient Consultation
  - Gastroscopy
  - Laparoscopic biliary (gallbladder) surgery
  - Laparoscopic anti-reflux surgery
  - Open and laparoscopic surgery for upper GI cancer
  - Open and laparoscopic pancreatic surgery (benign and malignant)
  - Laparoscopic surgery for morbid obesity (bariatric surgery)
  - Laparoscopic hernia repair

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Case 5 – Upper Abdominal Pain

- Underwent Cholecystectomy
- Now doing well

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Common GI and Liver Problems

- 1. NAFLD
- 2. Chronic Hepatitis C
- 3. Chronic Diarrhoea
- 4. Lower Gastro-intestinal (Colorectal)
- 5. Upper Gastro-intestinal (Upper Gastrointestinal)

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GI and Liver Solutions @ GLMS

- 1. NAFLD – *Hepatology Consultation, Fibroscan, Dietitian*
- 2. Chronic Hepatitis C – *Hepatology Consultation, Fibroscan*
- 3. Chronic Diarrhoea – *Gastroenterology Consultation, Gastroscopy and Colonoscopy, Dietitian, Bowel Cancer Screening Package*
- 4. Rectal bleeding clinic – *Colorectal Consultation, Flexible Sigmoidoscopy plus banding < 45y Consult plus Colon plus banding*
- 5. Upper Gastro-intestinal (Reflux, Gallstones) –*Upper GI Surgical Consultation, Gastroscopy*

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