A Symposium On The Latest Updates in Gastroenterology
Accredited 4 FM Core CME Points

BACK IN THE DAY

DIGESTIVE DISEASES

FOR THE FAMILY PHYSICIAN 2019

2nd November 2019, Saturday 12.00pm - 5.10pm
Hilton Singapore, Grand Ballroom

JAUNDICE

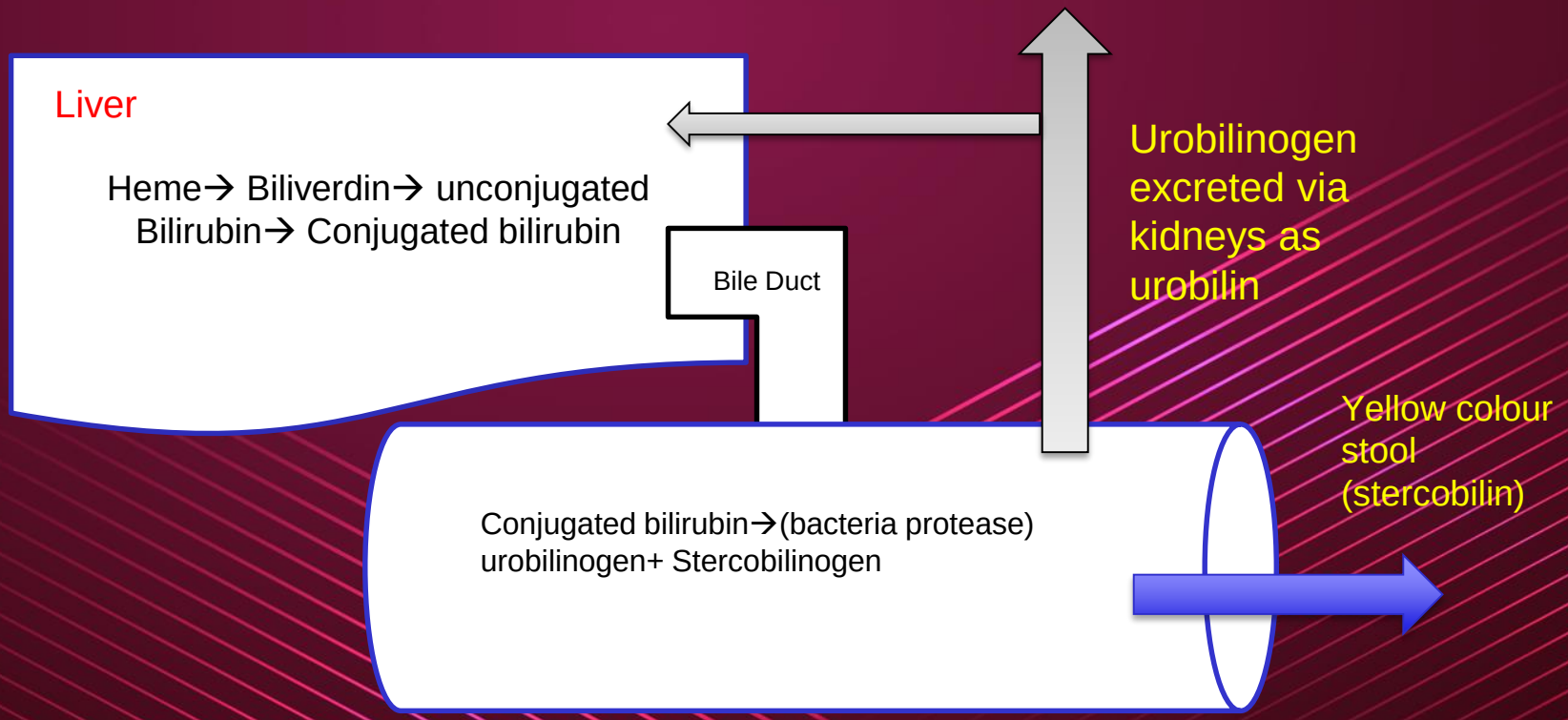
Dr Chong Chern Hao
Consultant Gastroenterologist

1) History of Jaundice
2) What are the causes of jaundice
3) How can I manage jaundice in primary care settings
4) When and how fast should I refer
5) Case discussion and Q&A

Objectives:
- Improve understanding of pathophysiology of jaundice and it's differential diagnosis
- Empower primary care practice in interpreting different types of jaundice
- Risk assessment and when you should consider to refer for further assessment

gutCARE
digestive • liver • endoscopy associates

Bilirubin Metabolism



gutCARE
digestive • liver • endoscopy associates

Evolution of Jaundice

3400 bc

460 bc first clinical features of jaundice and death

1836

Alcohol

1935

Obstruction

1940

Autoimmune /haemolysis

1950-1970

Hep A, B,E

Discovery of phototherapy

1970-1980

Hep C. D

Christian et al Liver Int 2014

gutCARE

digestive • liver • endoscopy associates

Classification of jaundice in Hippocratic Corpus(460bc)

Type 1	Type 2	Type 3	Type 4	Type 5
• Acute and rapidly fatal • Abdominal Pain after meal • Dies within 14 days	• Excessive heat of sun • Chills and fever, abdominal discomfort, stool foul smelling • Dies within 14 days	• Occurs in winter, drunkenness and chills • Body swelling • Prominent vessels on body • Better prognosis than type 2 but potentially fatal • Treatment by special diet and purging	• Excessive food intake or drunkenness • Chills, mild fever, weakness. • Better prognosis	• Occur mainly winter • Skin colour ashen • Cough/Sputum ++, rarely fatal • Treatment: Purging. Diet. baths • Good prognosis

gutCARE
digestive • liver • endoscopy associates

Hippocratic type of Jaundice

Type 1	Type 2	Type 3	Type 4	Type 5
• Acute and rapidly fatal • Abdominal Pain after meal • Dies within 14 days • Tx : Milk+Honey	• Chills and fever, abdominal discomfort, stool foul smelling • Excessive sun exposure • Dies within 14 days	• Occurs in winter, drunkenness and chills • Body swelling • Prominent vessels on body • Better prognosis than type 2 but potentially fatal • Treatment by special diet and purging	• Excessive food intake or drunkenness • Chills, mild fever, weakness. • Better prognosis	• Occur mainly winter • Skin colour ashen • Cough/Sputum ++, rarely fatal • Treatment: Purging. Diet. baths • Good prognosis
Hepatic Jaundice/Acute Liver failure	Post- Hepatic Jaundice, ? Acute cholangitis,	Chronic Liver disease/portal Hypertension	Acute viral hepatitis, ?alcoholic hepatitis cholelithiasis	? Renal disease/Uraemia ?Viral ? Systemic disease involving lungs

N Papavramidou J Gastrointest Surg 2007

gutCARE
digestive • liver • endoscopy associates

Classification of jaundice

Pre-hepatic

Red cells
haemolysis
Thalassemia
Toxin
Antibodies

Hepatic

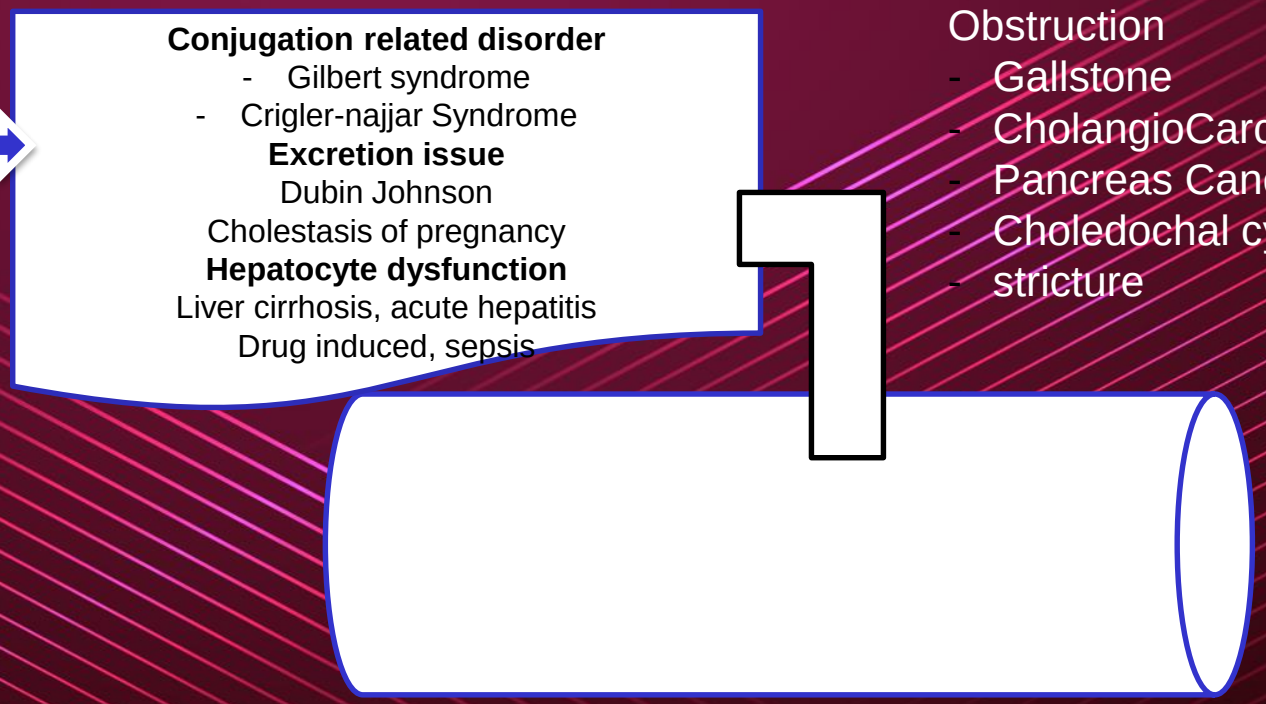
Conjugation related disorder
- Gilbert syndrome
- Crigler-najjar Syndrome

Excretion issue
Dubin Johnson
Cholestasis of pregnancy

Hepatocyte dysfunction
Liver cirrhosis, acute hepatitis
Drug induced, sepsis

Post Hepatic

Obstruction
- Gallstone
- CholangioCarcinoma
- Pancreas Cancer
- Choledochal cyst
- stricture



gutCARE
digestive • liver • endoscopy associates

Case 1 :

- 35 years old chinese women
- Vague upper abdominal pain for 2 weeks after meal
- On examination : Clinically jaundice, no stigmata of chronic liver disease.
- No travel history, No weight loss, no loss of appetite
- Denies fever

gutCARE
digestive • liver • endoscopy associates

Blood test

	13Oct16 01:56	15Oct16 09:56	15Oct16 10:02	16Oct16 04:56	17Oct16 08:16	17Oct16 14:12	18Oct16 11:27	19Oct16 06:36
Anion Gap	* ↑ 18.5	* ↑ 20.2						
Estimated Glomerular Filtration	* 129	* 114						
- Liver Function ---								
Alanine Aminotransferase	↑ 37	↑ 279		↑ 175	↑ 164		↑ 140	↑ 142
Aspartate Aminotransferase	↑ 70	↑ 124		↑ 62	↑ 69		↑ 57	↑ 71
Gamma Glutamyl Transpeptidase	↑ 108	↑ 331		↑ 244	↑ 247		↑ 212	
Total Protein, Serum	75	77		↓ 60	66		68	
Albumin	44	45		36	40		39	
Globulin	32	32		24	26		29	
Albumin:Globulin Ratio	1.39	1.40		1.50	1.52		1.34	
Bilirubin, Total	14	↑ 104		↑ 60	↑ 95		↑ 44	
Alkaline Phosphatase	89	↑ 231		↑ 176	↑ 190		↑ 170	
- Pancreatic Function ---								
Amylase	66	56					↑ 159	
- Sepsis Monitoring ---								
C-Reactive Protein				2.0	1.9			

gutCARE
digestive • liver • endoscopy associates

Clinical Approach to Jaundice in Primary Care

Key Consideration :

Is patient stable for outpatient care/work up?
Your comfort level looking patient with jaundice ?
Accessibility to early imaging and blood test for your patient?
The resources to review and manage this patient with a colleague(Gastroenterologist/Surgeon) who can support you when in doubt?
Early access for second opinion when waiting time is long ?

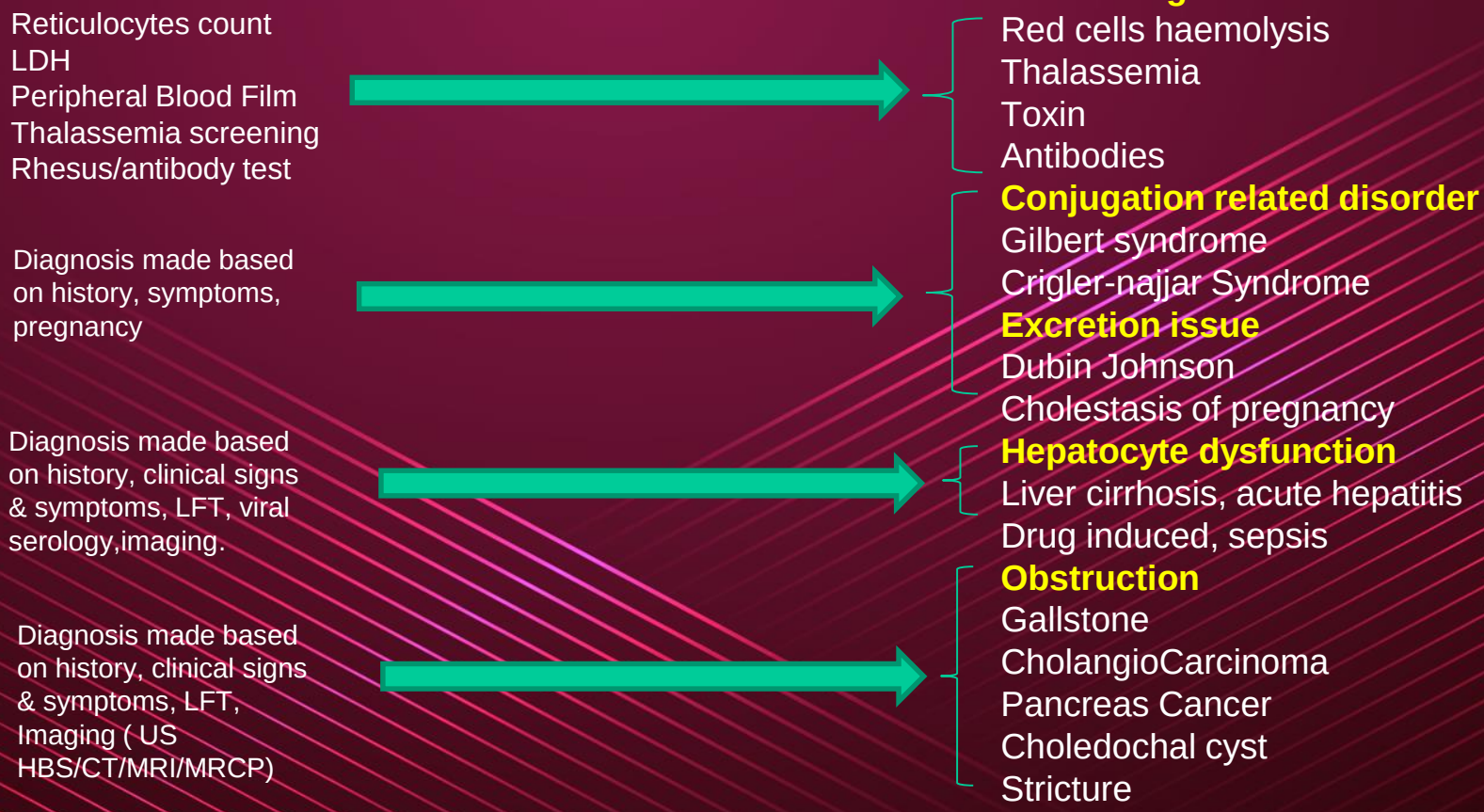
gutCARE
digestive • liver • endoscopy associates

Majority Jaundice can be work up as outpatient basis (within 1-2 weeks)

- If these patients are
  - Clinically well and stable not in sepsis
  - Not in pain/distress
  - Not in liver dysfunction (INR < 1.5, no hepatic encephalopathy)
  - Non Toxin/Paracetamol related
  - Non pregnancy related

gutCARE
digestive • liver • endoscopy associates

Accessibility to rapid imaging and diagnostic blood test



gutCARE
digestive • liver • endoscopy associates

Approach to Jaundice in primary Care

Physical examination and documentation
Look for

- signs of chronic liver disease
- risk factors for viral hepatitis
- Signs and symptoms suggestive of hepatobiliary cancer (constitutional symptoms)
- Drugs
- Signs of infection

Blood tests
FBC, LFT, Renal profile, PT/INR
Viral Hepatitis
Anti HAV IgM, HbsAg,
Anti HCV

Imaging
US HBS
CT Abdomen Pelvis + Pancreas
MRI/MRCP

Autoimmune work up
ANA/IGG/Anti SMA/AMA
Haemolysis panel : LDH, Reticulocyte counts, Haptoglobin(low)
Peripheral Blood film

Initial treatment for pruritus:
Topical urea cream
0.5-2% mentol + aqueous cream

gutCARE
digestive • liver • endoscopy associates

Ultrasound Hepatobiliary system

- Surface and Parenchymal characterization : hyperechoic (fatty infiltration), smooth, coarsened echotexture (fibrosis/cirrhosis), nodular appearance
- Lesion description : hyper/hypoechoic lesion/cyst, complex vs simple cyst, hypervascular (+ve Doppler signal)
- Biliary ductal system description : intrahepatic, common bile duct. Normal size < 5mm, +1mm with each decade. Dilated ducts seen post cholecystectomy. Echogenic shadows (Stone)
- Pancreas appearance, pancreatic duct size (< 3mm)

* Not able to visualize distal CBD very well due to duodenal air.

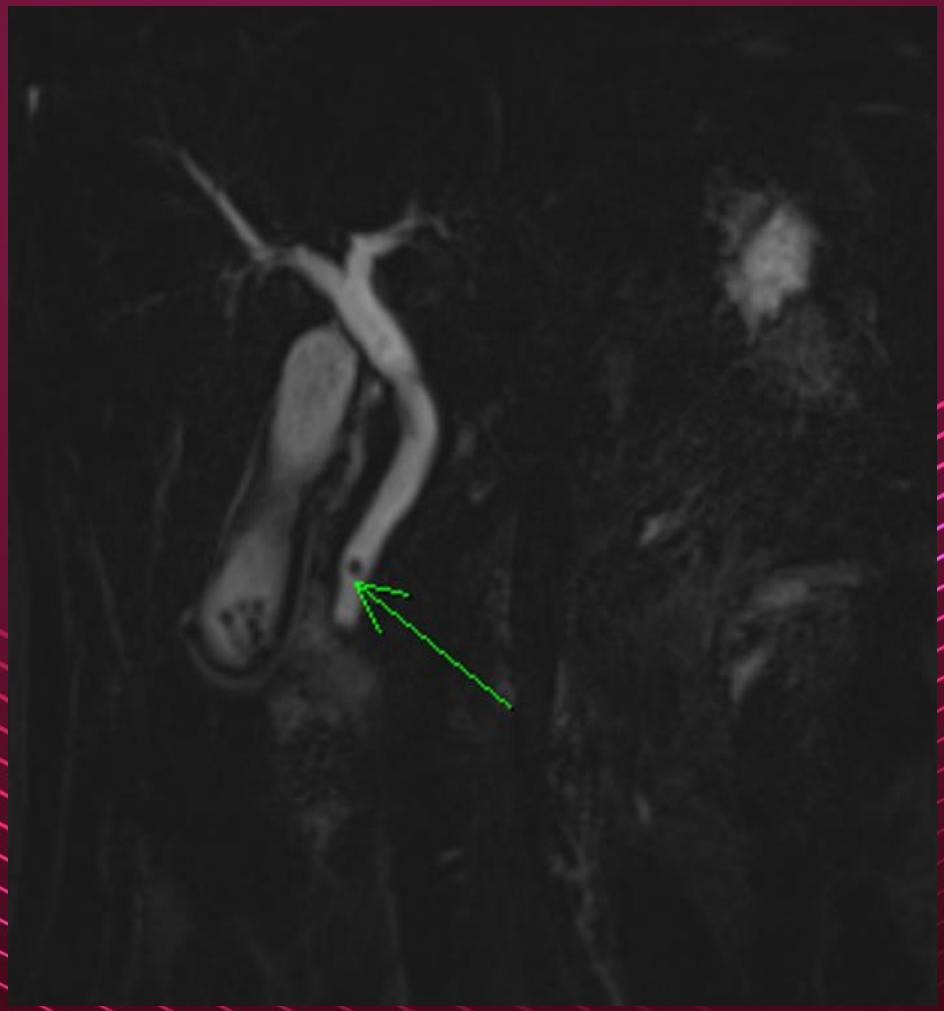
gutCARE
digestive • liver • endoscopy associates

Ultraround Hepatobiliary System provide a lot of information

- Cirrhosis
- Biliary duct obstruction (dilated biliary trees)
- Head of pancreas lesion
- Liver lesions

gutCARE
digestive • liver • endoscopy associates

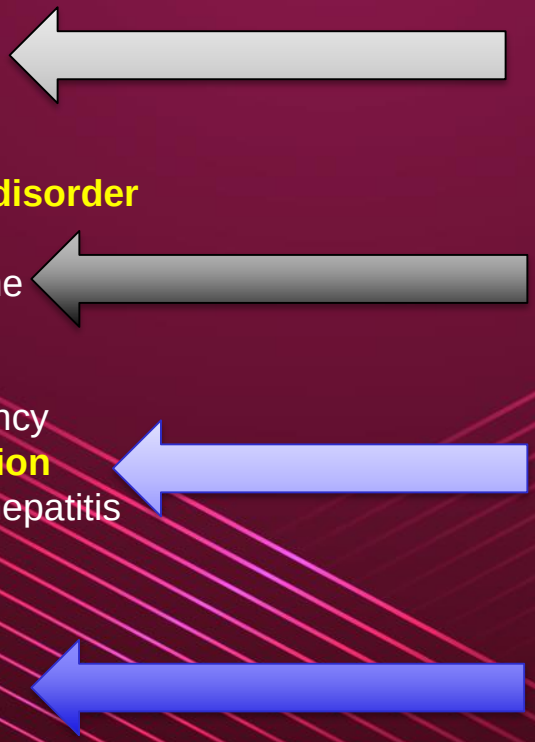
Case 1: MRCP



gutCARE
digestive • liver • endoscopy associates

Most Jaundice cases are medical related

List of diagnosis
Red cells haemolysis
Thalassemia
Toxin
Antibodies
Conjugation related disorder
Gilbert syndrome
Crigler-najjar Syndrome
Excretion issue
Dubin Johnson
Cholestasis of pregnancy
Hepatocyte dysfunction
Liver cirrhosis, acute hepatitis
Drug induced, sepsis
Obstruction
Gallstone
CholangioCarcinoma
Pancreas Cancer
Choledochal cyst
Stricture



Medical Related issue

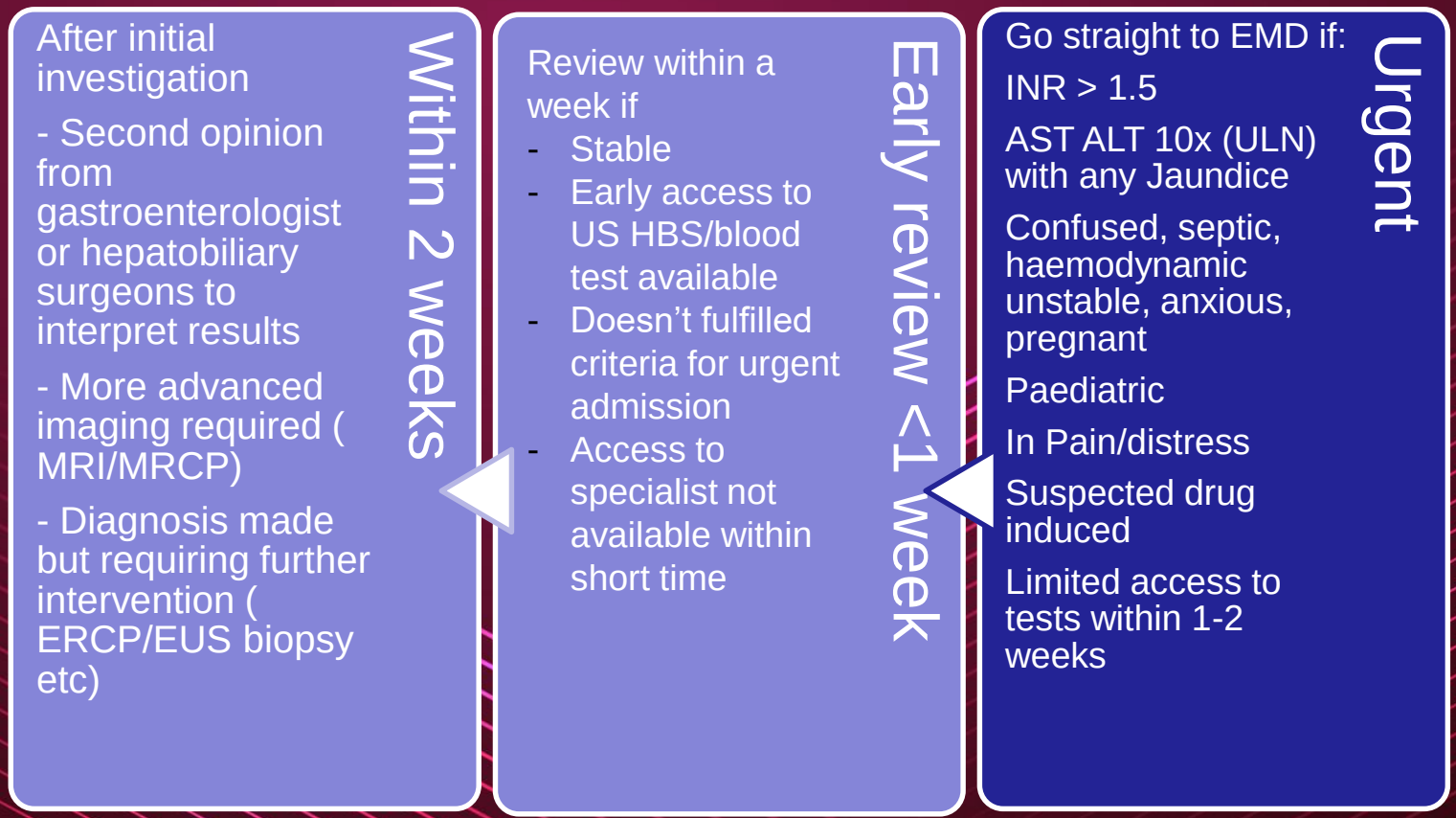
Medical Related issue

Medical Related issue

Surgical/Gastro Related issue

gutCARE
digestive • liver • endoscopy associates

Triaging cases from clinic :



gutCARE
digestive • liver • endoscopy associates

Role of gastroenterologist in managing biliary obstruction

Endoscopic stenting of biliary cancer/HOP cancer

ERCP mostly done by gastroenterologists

Obstruction

Gallstone
CholangioCarcinoma
Pancreas Cancer
Choledochal cyst
Stricture

Minimally invasive tissue biopsy via endoscopic ultrasound

gutCARE
digestive • liver • endoscopy associates

Case 2

- 28 years old female complaint of jaundice 1 week after taking antibiotics(bactrim) for UTI.
- On examination, she is jaundice with sclera icterus. No abdominal tenderness, No hepatosplenomegaly, no signs of chronic liver disease.
- There was no history of TCM, alcohol consumption.
- She has no medical/family history of chronic viral hepatitis or liver cancer.

gutCARE
digestive • liver • endoscopy associates

Blood tests

LFT
AST 70
ALT 65
ALP 403
Bilirubin 90

INR 1.2
Hb 12 TW 8
Platelet 200
Na 139 K 4 Urea 6 Creatinine 80

gutCARE
digestive • liver • endoscopy associates

Evaluation

- Rule out Hep B, C, AIH, Alcoholic liver cirrhosis, drugs, TCM
  - HbsAg, Anti HCV, immunoglobulin G, ANA, Anti SMA, history of alcohol consumption
- When to do Anti Mitochondrial Antibody? – Suspected PBC, raised ALP, bilirubin, female
- Rule out Wilson Disease – Eye screen for KF Ring, serum caeruloplasmin level, Urinary Copper
- Do metabolic markers – HbA1c, fasting sugar, lipid monitoring

Drug Induced Liver injury(DILI)

- Risk factors
- Women
- > 50 years old
- Multiple medication

- Hepatotoxicity via 2 pathways:
  - Direct toxic reaction
  - Idiosyncratic reaction
- 3 types
  - Hepatocellular
  - Mixed Pattern
  - Cholestatic

Common drugs associated with DILI

Drug Class or Drug	No. of Reports	ADR Description (No. of Reports)
Antilipid agents (eg, simvastatin, lovastatin, fenofibrate)	154	Transaminitis/LFTs abnormal (126), Hepatitis (25), Jaundice/Cholestatic hepatitis (3)
Antiepileptics (eg, phenytoin, carbamazepine, valproic acid)	22	Transaminitis/LFTs abnormal (11), Hepatitis (2), Transaminitis with rash/fever/systemic involvement (8), Hepatotoxicity (1)
Antituberculosis drugs (eg, isoniazid, rifampicin)	18	Hepatitis (10), Transaminitis/LFTs abnormal (5), Jaundice (1), Fulminant liver failure (1), Transaminitis with leukopenia (1)
Cotrimoxazole	10	Jaundice (3), Transaminitis (3), Transaminitis with haematological involvement (2), Hepatitis (2)
Allopurinol	7	Transaminitis/LFTs abnormal (2), Jaundice (1), Hepatitis and rash (1), LFTs abnormal and rash (1), Transaminitis with fever, rash, leukocytosis, eosinophilia (1)
Imidazole/Triazole Antifungals (eg, ketoconazole, itraconazole)	6	Transaminitis (2), Hepatitis with jaundice (2), Hepatitis (1), Hepatotoxicity (1)

HSA report 2009-2011

Current Recommendation

- ALT ≥ 3 times ULN or above patient's baseline or ALP ≥ 2 times ULN or above patient's baseline Any suspected case of DILI which does not improve with drug cessation should be referred to a specialist/tertiary centre.

- $R = \frac{ALT/ULN}{ALP/ULN}$

R >= 5 (hepatocellular)
R 2-5 (Mixed)
R <= 2 (Cholestatic)

Managing and Reporting Suspected DILI

- DILI is a presumptive diagnosis and many other liver disease need to be ruled out before establishing diagnosis.

What Relevant information should I include when referring to specialist/hospital?

- All concurrent drugs and dosages (including complementary medicine for the past 3 months)
- Start and stop dates
- Past medical history (particular chronic liver ds)
- Relevant ix (Labs, Imaging, serology work up for viral hepatitis)
- Alcohol use
- Drug challenge/rechallenge (if any)

Summary

- Jaundice Cases can be challenging to be manage in primary care, however, you can do more as first line investigator for your patient
- Your clinic resources, early access to blood tests, imaging tests determine how much you can do for your patient before referring patient for second opinion
- Giving your patient reassurance is extremely important

gutCARE

digestive • liver • endoscopy associates

Mount Elizabeth Novena Specialist Centre

Gleneagles Medical Centre

Parkway East Medical Centre

Mount Alvernia Hospital

Farrer Park Medical Centre

www.gutcare.com.sg