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Objective One

In a patient presenting with hepatitis symptoms and/or abnormal liver function tests, take a focused history to assist in establishing the aetiology.

When hepatitis is suspected based on physical or labs, be sure (as always) to perform a very thorough H&P. In particular, ask about symptoms or signs that may indicate liver disease, such as:

- nausea & vomiting
- abdominal pain
- anorexia
- malaise, fevers & chills
- recent weight loss
- jaundice, dark urine, or light coloured stools
- Palmar eryhema and pruritus

Next up, always assess for medical conditions and comorbidities:

If a patient presents with elevated liver enzymes and also has obesity, diabetes or hyperlipidaemia, make sure nonalcoholic fatty liver disease is on your differential since this is a rising cause of liver disease and can ultimately lead to cirrhosis and liver failure.

Ask about a personal or family history of inflammatory or autoimmune disease.

Keep in mind the possibility of hemochromatosis and other infiltrative processes. In Central Newfoundland where I'm training hemochromatosis is actually relatively common.

Medication History

ask about use of hepatotoxic medications and substances. There is a huge list of things people take that can hurt the liver and we can't go over them all here. But be sure to keep in mind the common offenders. Tylenol is a classic so be sure to get a good grasp on how much someone may be taking daily.

Other culprits are the NSAIDs, statins, some -azole antifungals, anticonvulsants, and common antibiotics like amoxicillin, nitrofurantoin, and sulfonamides

But these are not all so keep a critical eye on the med list, including OTCs and herbals. Pro-tip: if you're unsure about the hepatotoxicity of a drug you can use LiverTox.nih.gov for a complete up-to-date listing.

Link to searchable LiverTox database here > Information and Search Database

Social History

For alcohol use, try to pin the patient down to the type of drink, drinking pattern, and the weekly or daily averages. The definition of "one drink" will vary wildly from one patient to the next.

Ask about behaviours associated with increased risk of viral hepatitis, such as current or past IV drug use, high risk sexual behaviour, non sterile piercings or "homemade tattoos", and accidental needle sticks or cuts. Remember too that being born a baby boomer is itself a risk factor (that's between 1945-1965).

Sexual transmission is a key vector for most of the infectious hepatidities so ask *dirtectly* about higher risk sexual activity, including having multiple sexual partners, condom use, and in men who have sex with men.

Ask about Vaccination status if known!

Ask if they've recently visited or have lived in endemic areas where there may be a higher likelihood of contaminated water sources - remember Hepatitis A and E are both spread this way through the faecal-oral route.

Finally, the objective doesn't mention it but the physical exam is always important. Here you want to look for the obvious things like scleral icterus or jaundice, hepatomegaly, RUQ pain;

and also some of the specialised stuff like: palmar erythema, telangiectasias, caput medusae, ascites and testicular atrophy. Although these are relatively late-findings.

Objective Two

In a patient with abnormal liver enzyme tests interpret the results to distinguish between obstructive and hepatocellular causes for hepatitis as the subsequent investigation differs.

Before we get into Liver enzyme and function test interpretation, remember that none of the tests are specific for liver disease but the overall pattern can provide some clues as to the type of liver injury. So, don't hang your hat on a diagnosis based on labs alone and avoid anchoring early in the workup.

Here's a quick refresher of the biomarkers you need to know:

1. AST & ALT - aka: the transaminases - generally these will point you towards a *hepatocellular* insult. These enzymes live in the hepatocytes and spill out when the cells become damaged. Remember though that while ALT is more liver specific, neither are exclusive to hepatocytes; AST in particular is also found in cardiac & skeletal muscle and can be elevated in other disorders such as celiac & thyroid disease.
2. Next up, ALP (aka: alk phos), this points to a *cholestatic* type pattern when elevated. And It's also present in bone, intestines, kidney, and placenta.
3. GGT - (Gamma Glutamyl Transpeptidase) this guy lives on the surface of hepatocytes and biliary epithelia, but unlike Alk Phos it is not found in bone. This makes it a useful test to confirm that an Alk Phos elevation is actually coming from the liver and not from another process like bone turnover or bone mets.
4. Bilirubin - this is a product of heme metabolism. It's conjugated in the liver and excreted in bile. Remember that direct=conjugated, indirect=unconjugated and that the sum of both is your total bili.
    a. High indirect bili can be evidence of either impaired bilirubin conjugation or of increased hemolysis.

   b. High direct bili can be evidence of either cholestasis or hepatocellular damage.
5. Finally we can't forget the true markers of synthetic function: Albumin, PT/ INR, and Platelets. Remember that while an elevated PT can be an early marker of injury, a decreased albumin usually takes a little longer to show; and it can go down with losses due to nephrotic syndrome or malnutrition.

So in short:
Think Hepatocellular if the Transaminases are up.
Think Cholestatic if the Alk Phos is up and confirm with GGT.

For a validated shortcut to decide whether the pattern is hepatocellular or cholestatic, you can use the ALT and ALP levels to calculate the "R-factor" on MDCalc or another similar app. And It's recommended by the most recent ACG guidelines.

Also always consider the AST:ALT ratio. alcoholic liver disease is suggested with an AST:ALT ratio greater than 2; if this ratio is present it yields a likelihood ratio of 17!

Objective Three
In a patient where an obstructive pattern has been identified,
a) Promptly arrange for imaging,
b) Refer for more definitive management in a timely manner.

People tend to present commonly in the ER for this issue. They will classically present early on with colicky RUQ pain and a positive Murphy's sign. Also remember from your clinical skills days to look for *Charcot's triad* of: RUQ pain with fever and jaundice which indicates possible cholecystitis; and *Reynauld's pentad* with the addition of hypotension and confusion; this of course signals the dreaded Ascending Cholangitis.

In any case, when your differential includes biliary colic or stones you'll certainly order a set of LFTs which will likely show high ALP and Bili, plus or minus GGT if it was ordered. If you see this along with your expert physical findings then proceed directly to RUQ U/S.

You'll be looking for many things but focus on the presence or absence of biliary dilatation to differentiate extrahepatic from intrahepatic cholestasis.

If ductal dilatation is present:
Consider choledocolithiasis and consult GI for further management. Alternatively, gen surg may be your next go to consult depending on where you are and the resources you have. Other considerations include cholangiocarcinoma or pancreatic cancer; In which case you'll want to arrange a CT or MRI with a referral.

If no ductal dilation is present then consider medications, alcohol, the viral hepatitides, primary biliary cholangitis, and all the various and sundry infiltrative processes that you'll likely need to look up at this point.

Objective Four
In patients positive for Hepatitis B and/or C,
a) Assess their infectiousness,
b) Determine human immunodeficiency virus status.

Hepatitis serologies can get very confusing very fast if you're trying to memorise the tables, so this may not be worth the squeeze for something you can look up fairly easily. we'll try to just touch the highlights here.

For Hepatitis B screening and diagnosis,
Generally, we want to screen those who are at high risk for infections and complications. Pregnant women are generally screened as part of routine prenatal care. Other people you may want to screen include those who are Hep C positive, are HIV positive, those on chemo or starting immunosuppressants, and those with chronically high liver enzyme elevations.

The lab markers to look for to diagnose an ***acute*** infection are a positive Hep B surface antigen (HBsAG) & **IgM** antibody to Hepatitis core antigen (IgM anti-HBc)

For ***chronic*** infection, the markers will still show a positive surface antigen, but the immunoglobulin will now switch from **IgM** to **IgG**, and you might still see a positive Hepatitis B **e antigen** but this can vary**.**

Next, to determine infectiousness look at the serologies. In hep B a highly infective patient will have positive surface antigen, core antigen IgM, & E antigen. The patient will lose E antigen positivity at some point after transitioning to the chronic phase, and will be considered less infectious. In general though, the presence of the surface antigen indicates they are infectious to some degree.

Objective Five
In patients who are Hepatitis C antibodies positive determine those patients who are chronically infected with Hepatitis C, because they are at greater risk for cirrhosis and hepatocellular cancer.
And
Objective Seven
In patients who are at risk for Hepatitis B and/or Hepatitis C exposure,
a) Counsel about harm reduction strategies, risk of other blood borne diseases,
b) Vaccinate accordingly.

The CDC recommends universal screening for Hep C in all adults over 18; however, The Canadian Task Force on Preventive Health Care, the WHO, and the most recent 2018 guideline from the Canadian Association for the Study of the Liver all recommend screening for HCV infection in people who are at higher risk only.

These groups include: IV and intranasal drug users; prisoners or the recently incarcerated; people with HIV; people whose sexual partners are infected with HCV; people who have had tattoos or piercings; and individuals who were born in, have traveled to, or have lived in a country where HCV is endemic.

In addition, the CDC and Canadian liver foundation include those born between 1945 & 1965 - aka the baby boomers - as a high risk group who should receive one-time screening.

Link to screening infographic here > Hepatitis C Screening & Testing Quick Reference Guide

A high proportion of Canadians with chronic HCV infection remain undiagnosed so screening everyone who is eligible is more important than ever since new treatments can cure almost everybody in 8 to 12 weeks!

Patients with Hepatitis C are diagnosed after they test positive for both the HCV Antibody screen and reflexive HCV RNA serologies.

After diagnosis, these patients need counselling on some specific preventative measures they can take to protect their health and that of others.

1. Make sure they are up to date on immunizations for Hepatitis A and B. Also get them a Tdap, annual influenza and pneumovax.
2. Be sure to screen for coinfections, especially HIV, HBV and STIs.
3. Unlike those patients with Hep B, screening for HCC (hepatocellular carcinoma is only indicated in those with confirmed cirrhosis - this is done as a Q 6 monthly liver ultrasound.
4. Retesting should be performed at least once per year in those individuals who are engaged in ongoing high-risk activities and must be done with HCV RNA.

Finally, patient education should make up a big part of visits with these patients, so when you can, be sure to cover.

1. Preventing infecting others:
    a. Discuss modes of transmission which include via: blood, sex and vertical transmission.
    b. Counsel on avoidance of blood donation or other activities that can expose others to the blood of the patient.
    c. Advise HBV vaccination of close contacts .
2. To help prevent disease progression in those chronically infected:
    a. Avoid other risk factors for liver injury such as alcohol, tobacco, and obesity.

b. Avoid NSAIDs and limit Acetaminophen to less than 2 grams per day.
c. 3 or more cups of coffee per day may reduce progression to HCC

Also, for those patients infected with hepatitis B, the REACH-B score (which stands for Risk Estimation For HCC in Chronic Hepatitis B) can offer an objective measure of determining their risk of progression to HCC.

Objective Six

In patients who are chronically infected with Hepatitis C, refer for further assessment and possible treatment.

Per the Canadian guidelines, all patients with chronic hep C infection should be considered candidates for antiviral therapy. Prompt initiation of treatment should occur, especially in your patients with advanced liver fibrosis

The guidelines also suggest that all individuals who test positive for HCV RNA be evaluated by practitioners with experience in hep C management. There seems to be a push on now for the expansion of nonspecialist HCV care which will be required in Canada to ensure that all infected individuals receive appropriate care.

There are resources available in certain provinces such as project ECHO which helps primary care co-manage these patients with experienced providers and is a useful tool to look into for those who have access to it.

Also, if you need backup, the Canadian Liver Foundation keeps a running list of physicians who treat Hep C in Canada, so if you feel a little out of your wheelhouse then check out their directory at Liver.ca

(URL here > https://www.liver.ca/professionals/health-professionals/#diagnostics)

Objective Eight

Offer post-exposure prophylaxis to patients who are exposed or possibly exposed to Hepatitis A or B.

For hepatitis A postexposure prophylaxis, we would give both hepatitis A immunoglobulin and the first dose of the vaccine. This combo should be given to household and intimate contacts within 2 weeks of exposure.
The effectiveness of the hepatitis A vaccine exceeds 90%, and is administered as 2 doses given 6 months apart.

The Hepatitis B vaccine also confers effective immunity in over 90% of patients. It is given in 3 doses over 6 months. It should be standard for health care workers, and should be given to all children in Canada routinely.

For Hepatitis B postexposure prophylaxis, the Hep B immunoglobulin is given at the same time as the first dose of vaccine for those who have had a recent exposure. For example, a needle stick or for newborns of infected mothers.

Unfortunately, there are no current vaccines or effective post exposure prophylaxis for available Hepatitis C.

Objective Nine

Periodically look for complications in patients with chronic viral hepatitis, especially hepatitis C infection.

Since chronic hepatitis can lead to both cirrhosis and hepatocellular carcinoma you'll want to stay on top of screening these patients.

For untreated hep B Infection: all patients should have regular monitoring of ALT every 6 months and HBV DNA every 6–12 months.

Then a repeat fibrosis assessment may be indicated if persistent ALT elevation and HBV DNA are present to assess the need for treatment. Liver biopsy was gold standard for Fibrosis assessment, but 2018 guidelines state that fibrosis can be evaluated adequately with either elastography or by calculating a FIB4 score.

FIB-4 Link > calculator

For Hep C The 2018 guidelines from the Canadian Association for the Study of the Liver recommend no specific liver-related follow-up in those patients who are cured *and do not* have cirrhosis. In those with ongoing risk exposures, they suggest annual HCV RNA testing to assess for reinfection.

For patients who have cirrhosis before the start of hepatitis treatment, ongoing follow-up is required. Surveillance for hepatocellular carcinoma with Q 6 monthly ultrasound should be continued indefinitely after sustained virologic response, even if noninvasive tests no longer suggest the presence of cirrhosis

When looking after patients with cirrhosis, you can use a few different calculators to assess disease severity & prognosis . The Child-Pugh score was the original, but today you'll more commonly hear about the MELD (Model for End Stage Liver Disease) or PELD score for patients younger than 12. Both the MELD and the PELD are used to prioritise liver transplant, so it's critical to know where your patients stand.

Finally, In your cirrhotic patients don't forget to include counselling on things they can do to optimise their health for themselves. Nutrition can be a big part of that and cirrhotics need special guidance in that department. The "Nutrition in Cirrhosis Guide" is a peer reviewed resource out of the University of Alberta that can be very helpful in this regard and is available for free to your patients and yourself.

It's linked > here

Along with the typical articles & guidelines, much of the medical info in this episode comes from “A Textbook on Clinical Hepatology”, the free e-book and PDF are available through the Canadian Liver Foundation website and is linked here. > https://www.hepatologytextbook.com

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Guidelines

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