30 – Acute Hepatitis

Speaker: David Thomas, MD

IDBR INFECTIOUS DISEASE BOARD REVIEW AUGUST 20-24 2022

Acute Hepatitis

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7/10/2022

IDBR INFECTIOUS DISEASE BOARD REVIEW AUGUST 20-24 2022

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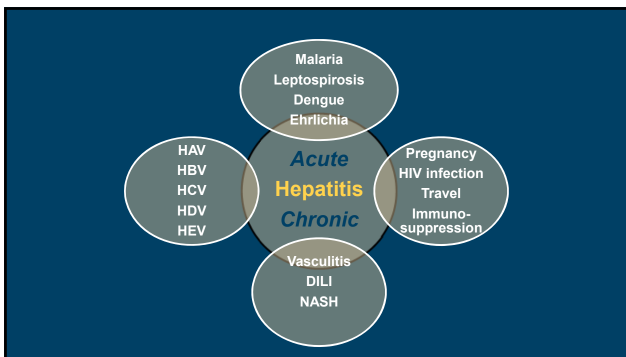

18 year-old with jaundice

- 18 y/o presents with 5d of headache, fever, diarrhea, vomiting, chest pain
- PMH – Open fractures of all R metatarsals with pins x 3mo
- SH – home tattoos; lives with parents and pregnant girlfriend; dogs and rats; swam in freshwater dam 1 wk before symptom onset; cuts grass; multiple tick bites; Maryland

Courtesy E Prochaska, MD

18 year-old with jaundice, con't

- T 39.4; BP 118/62 (then on pressors); P 91; 97% RA
- Icteric, non-injected, no murmurs
- Diffuse petechial rash; purple macules on ankle
- WBC 11,740 (92.4 P, 0.8B, 2% L); Hb 14.2; Plt 47,000
- Creatinine 0.9-3.4; CRP 10.1; Tbili 4.1 (direct 3.7); ALT/AST 26/53; CK 887
- HIV Ab neg; SARS-CoV-2 PCR neg; Monospot - neg

Courtesy E Prochaska, MD

18 year old with jaundice

The cause of his illness is:

A. Acute hepatitis A
B. Babesia microti
C. Tularemia
D. Leptospira icterohaemorrhagiae
E. HSV

Courtesy E Prochaska, MD

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Leptospirosis

1. **Exposure to fresh water (eg rafting in Hawaii/Costa Rico or triathlon) OR rats (Baltimore)**

Leptospirosis

2. Bilirubin fold change > ALT

Leptospirosis

3. Biphasic possible and systemic findings
(conjunctival suffusion, kidney, skin, muscle, lungs, liver)

ddx: liver and muscle: **flu, adeno, EBV, HIV, malaria, Rickettsia/Ehrlichiosis, tularemia, TSS, coxsackie, vasculitis**

Leptospirosis

4. Diagnosis:

- PCR most useful (urine pos longer)

- serology late

2022 PREVIEW QUESTION

Acute Hepatitis in Uganda

- 42 year old female has malaise and RUQ pain; she just returned from 2 months working at an IDP camp in north Uganda. She endorses tick and other 'bug' bites and swam in the Nile. 1st HAV vaccine 2 days before departure. Prior HBV vaccine series.
- Exam shows no fever, vitals are normal. RUQ tender. Mild icteric. ALT 1245 IU/ml; Hb 13.4 g/dl; TB 3.2 mg/dl; WBC 3.2k nl differential.

2022 PREVIEW QUESTION

Acute hepatitis in Uganda

Which test result is most likely positive?

A. Ebola PCR
B. IgM anti-HEV
C. IgM anti-HAV
D. Schistosomiasis "liver" antigen
E. 16S RNA for Rickettsial organism

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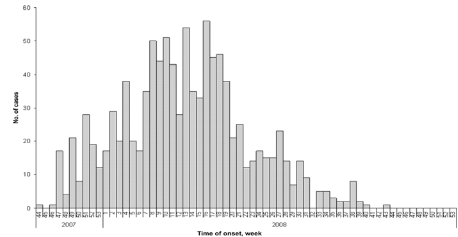
1. Vaccination works vs immune globulin to prevent hepatitis A *up to 14d after* exposure

End Points	Per-Protocol Population		Modified Intention-to-Treat Population†	
	Vaccine Group (N=568)	Immune Globulin Group (N=522)	Vaccine Group (N=740)	Immune Globulin Group (N=674)
	number (percent)			
Clinical				
Primary				
Any symptom plus IgM-positive and ALT ≥ twice ULN	25 (4.4)	17 (3.3)	26 (3.5)	18 (2.7)
Secondary				
Any symptom plus IgM-positive and ALT ≥ twice ULN or HAV RNA–positive on PCR‡	29 (5.1)	19 (3.6)	30 (4.1)	20 (3.0)
Jaundice plus IgM-positive and ALT ≥ twice ULN or HAV RNA–positive on PCR	18 (3.2)	12 (2.3)	19 (2.6)	12 (1.8)

Victor NEJM 2007

2. There are HEV outbreaks, eg. North-Ugandan IDP Camp



Teshale CID 2010

3. Hepatitis E: Epidemiologic Clues

- –Outbreaks – contaminated water in Asia/Africa
- –Sporadic - undercooked meat (BOAR, deer, etc)
- –Overseas travel typical
- –USA: endemic rare, genotype 3, IgG serology positive far more than can be explained by cases - can be hard to interpret

4. Hepatitis E: Clinical Clues

- –Fatalities in pregnant women
- –Can be chronic in transplant (rarely in HIV)
- –GBS and neurologic manifestations (vs other hep viruses); pancreatitis
- –Diagnosis: RNA PCR; IgM anti-HEV
- –Treatment: ribavirin for chronic

Acute Hepatitis at ID Week

- 42 year old homeless male approaches a group of ID fellows while attending ID Week in San Diego.
- One fellow noticed jaundice and suggested he seek medical testing. With what diagnosis was the fellow most concerned?

Acute hepatitis at ID week

Fellow worried about?

A. HAV
B. HBV
C. Delta
D. HCV
E. HEV

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1. Hepatitis A: Key Epidemiologic Clues – People, Places and Foods

Homelessness and Hepatitis A—San Diego County, 2016–2018

Corey M. Peak,[1,2,3] Sarah S. Stous,[2] Jessica M. Healy,[4] Megan G. Hofmeister,[5] Yulin Lin,[5] Sumathi Ramachandran,[5] Monique A. Foster,[5] Annie Kao,[2] and Eric C. McDonald[2]

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Morbidity and Mortality Weekly Report (*MMWR*)

CDC > MMWR

Notes from the Field: Increase in Reported Hepatitis A Infections Among Men Who Have Sex with Men — New York City, January–August 2017

Weekly / September 22, 2017 / 66(37);999–1000

1. Hepatitis A: Key Epidemiologic Clues – People, Places and Foods

Multistate Outbreak of Hepatitis A Linked to Frozen Strawberries – Current Case Count Map and Table

Posted December 16, 2016 2:30 PM ET

Case Count as of December 13, 2016

tropical SMOOTHIE CAFE
eat better. feel better.

State	Case Count
Arkansas	1
California	1
Maryland	12
New York	5
North Carolina	4
Oregon	1
Virginia	109
West Virginia	7
Wisconsin	3
Grand Total	143

Outbreak of hepatitis A in Hawaii linked to raw scallops

Posted August 19, 2016 5:00 PM ET

Outbreak

The Hawaii Department of Health (HDOH) is investigating an outbreak of hepatitis A in its state. For the latest case count and investigation findings, visit the HDOH outbreak investigation website. On August 15, 2016, HDOH identified raw scallops served at Genki Sushi restaurants on the islands of Oahu and Kauai as a likely source of the ongoing outbreak.

CDC and the U.S. Food and Drug Administration (FDA) are assisting HDOH with its investigation. At this time, CDC is not aware of any hepatitis A virus infections in other states linked to the Hawaii outbreak. CDC continues to monitor for illnesses in other states.

2. Hepatitis A: Key Clinical Clues

- There are outbreaks all over the world
- The most common cause of acute hepatitis in USA
- Clinical syndrome
  - fulminant on HCV
  - relapsing: symptoms/jaundice recur <12 mo

3. Vaccination to Prevent Hepatitis A

- ***Pre-exposure:*** **vaccinate**
  - HOW: Inactivated vaccines USA (HAVRIX,VAQTA)(TWINRIX)
  - WHOM: HCV or HBV positive persons/chronic liver disease/homeless/MSM/PWID/Travelers/HIV pos/adoptee exposure
  - All children 1-18 yrs receive hepatitis A vaccine (since 2006)
- ***Post-exposure:*** **vaccinate (and possibly IG)**
  - Unless > 40 years or immunosuppressed then IG is 'preferred'
  - Close exposure (sex or IDU partner) not casual (eg office worker)

Victor NEJM 2007; MMWR July 3 2020; MMWR October 19, 2007 / 56(41);1080-1084

Acute Viral Hepatitis B Clues

- Most linked to sex, drugs, nosocomial
  - Nosocomial (fingerstick devices, etc)
  - Most transmissible (HBV>HCV>HIV)
- Clinical
  - Acute immune complex disease possible
  - Diagnose: IgM anti-core, HBsAg and HBV DNA
  - New infection vs reactivation (both can be IgM pos)

More on HBV

- See lecture on chronic hepatitis for prevention, HIV coinfection, and treatment

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Acute Viral Hepatitis Delta will be with HBV

- HDV
  - –HBV coinfection
    - Fulminant with acute HBV
  - –HBV superinfection
    - Acute hepatitis in someone with chronic HBV
  - –Test for HDV RNA

Acute Viral Hepatitis C clues

- HCV
  - –IDU link (hepatitis in Appalachia)
  - –HIV pos MSM
  - –Acute RNA pos but AB neg or pos
  - –60-80% persist: more in men, HIV pos, African ancestry, INFL4 gene intact

Cox CID 2005

Hepatitis in a pilot

- 70 y/o pilot presents with 1 week of fever, diarrhea and sweats, then "collapses"
- Tooth extraction 1 month before, E. Shore of Maryland and extensive travel, chelation "treatment"
- T 38.1, 135/70, 85, 18, 97% on 2L; few small nodes, petechial rash on legs, neuro- WNL

Pilot Case History, con't

- Hct 33%, WBC 1.4 K (81% P 10% L), Plt 15,000
- Creat 2.8
- AST 495, ALT 159, Alk Phos 47, alb 2.6, TBR 0.8
- CPK 8477
- CXR: infiltrate LLL

Hepatitis in a pilot

What agent caused this illness?

A. Leptospira icterohaemorrhagiae
B. Hepatitis A
C. EBV
D. Ehrlichia chaffeensis
E. Hepatitis G (GB virus C)

Hepatitis with bacterial infections

1. Think Rickettsia/Ehrlichia with exposure, low PMN, and especially low platelets

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Hepatitis with bacterial infections

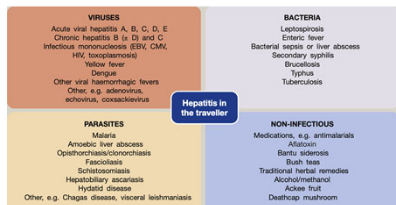
2. Coxiella burnetti and spirochetes (syphilis and lepto) also in ddx with liver, lung, renal, skin, CNS disease but tend to be cholestatic vs Rickettsia/Ehrlichia

Hepatitis with bacterial infections

3. Hepatitis F or G are WRONG answers

Hepatitis with travel to developing country

There is a broad differential



Jones Medicine 2017

Hepatitis with travel

Especially remember dengue (below), Chickungunya, or Zika

Ref.	Patients	Raised AST	Raised ALT	AST > ALT	Hyper-bilirubinemia	> 10 fold rise (AST, ALT)
Kuo et al[37]	270	93.30%	82.20%	+	7.20%	11.1%, 7.4%
Souza et al[39]	1585	63.40%	45%	+	-	3.4%, 1.8%
Itha et al[41]	45	96%	96%	Equal	30%	-
Wong et al[40]	127	90.60%	71.70%	+ in 75.6%	13.4%	10.2%, 9.5%
Parkash et al[33]	699	95%	86%	+	-	15%
Trung et al[36]	644	97%	97%	+	1.7%	-
Lee et al[14]	690	86%	46%	-	-	1%
Karoli et al[34]	138	92%		+	48%	-
Saha et al[35]	1226				16.9%	

Samanta World J Cases 2015

Hepatitis in Pregnancy

- 25yo G1P1 34 wks gestation with 1wk fever, chills, abd pain. 1 wk earlier cephalexin for GpB Strep.
- T 102; other vitals and exam as expected
- Plt 143K; Hb 8.6; WBC 6.4K 20% bands; glucose, creat and INR WNL; ALT 279; AST 643; TB 0.8.
- Hosp day 4:PLT 83K; PT 16; PTT 44; AST 2,240; ALT 980; BR nl; Fibrinogen NL;

Allen OB GYN 2005

Hepatitis in pregnancy

What is the best diagnosis?

A. HELLP
B. Acute fatty liver of pregnancy
C. Atypical DRESS from cefelexin
D. HSV infection
E. HEV

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Hepatitis in pregnancy

1. Rule out HSV

~50% have muco-cutaneous lesions

High mortality without acyclovir

Pregnant woman: initial workup of abnormal liver tests

Hepatocellular profile? AST/ALT

Rule out: Viral hepatitis Herpes Medications Other**

Anti-HAV IgM HBsAg Hepatitis E IgM HSV PCR

See Pregnancy-related workup

Biliary profile? elevated bili/alk phos

Bilirubin +/– alk phos

Alk phos only

Biliary imaging

No further workup

No evidence of obstruction

Figure 1. Workup of abnormal liver test in pregnant woman. **Other differential diagnosis to consider if clinically appropriate: AIH, Wilson disease.

ACOG 2016

Hepatitis in pregnancy

2. HELLP
   - HTN and can occur post partum
   - Fibrinogen high vs. sepsis and AFLP

3. AFLP – severe and low glucose, inc INR, low fibrinogen (Swansea criteria)

Fulminant hepatitis

- 65 year old man with hx of jaundice. 2 weeks before finished amoxacillin/clavulanate acid for sinusitis. Hx of HTN on HCTZ and rosuvastatin. ETOH: 2 drinks per day.
- TB24; ALT 162 U/L; AST 97 U/L ALK P 235 U/L. IgM anti-HAV neg; IgM anti-HBc neg; HCV RNA neg. RUQ US neg.

Fulminant Hepatitis

Which of the following is the most likely cause of hepatitis:

A. toxicity from amox/clav
B. alcohol
C. porphyria flare
D. leptospirosis
E. statin

Drug related liver toxicity

Amoxicillin/clavulanate is most common
- Cholestatic or mixed
- Often AFTER stopping
- 1/2500 Rx
- DRB1*1501
- clavulanate>amoxicillin

Rank	Agent	Year of FDA Approval	No. (%)†	Major Phenotypes
1	Amoxicillin–clavulanate	1984	91 (10.1)	Cholestatic or mixed hepatitis
2	Isoniazid	1952	48 (5.3)	Acute hepatocellular hepatitis
3	Nitrofurantoin	1953	42 (4.7)	Acute or chronic hepatocellular hepatitis
4	TMP-SMZ	1973	31 (3.4)	Mixed hepatitis
5	Minocycline	1971	28 (3.1)	Acute or chronic hepatocellular hepatitis
6	Cefazolin	1973	20 (2.2)	Cholestatic hepatitis
7	Azithromycin	1991	18 (2.0)	Hepatocellular, mixed, or cholestatic hepatitis
8	Ciprofloxacin	1987	16 (1.8)	Hepatocellular, mixed, or cholestatic hepatitis
9	Levofloxacin	1996	13 (1.4)	Hepatocellular, mixed, or cholestatic hepatitis
10	Diclofenac	1988	12 (1.3)	Acute or chronic hepatocellular hepatitis
11	Phenytoin	1946	12 (1.3)	Hepatocellular or mixed hepatitis
12	Methyldopa	1962	11 (1.2)	Hepatocellular or mixed hepatitis
13	Azathioprine	1968	10 (1.1)	Cholestatic hepatitis

http://livertox.nlm.nih.gov; Hoofnagle NEJM 2019

Acute Hepatitis Summary

- Acute A: vaccine effective
- HEV: chronic in transplant and/or boar
- HIV: acute HCV in MSM
- Ehrlichial or rickettsial
- Find the lepto case (jaundice>hepatitis)

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Thanks and good luck on the test!

Questions:

Dave Thomas

–dthomas@jhmi.edu

BREAK

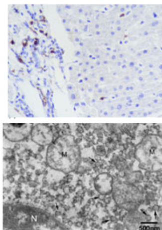
SLIDES BEYOND THIS ARE FOR THE PRESENTER'S RECORDS; NOT TO BE DISTRIBUTED OR SHOWN

Hepatitis in 2020: SARS-CoV-2

Table 2. Laboratory and radiographic findings of patients with COVID-

	All patients (N = 788)
Leukocytes, $\times 10^9$/L	4.8 (3.8–6.0)
Neutrophils, $\times 10^9$/L	3.0 (2.2–4.0)
Lymphocytes $\times 10^9$/L	1.2 (0.9–1.6)
$\geq 0.8 \times 10^9$/L	654 (83.0)
$< 0.8 \times 10^9$/L	134 (17.0)
Platelets, $\times 10^9$/L	181 (147–221)
$\geq 100 \times 10^9$/L	761 (96.6)
$< 100 \times 10^9$/L	27 (3.4)
Hemoglobin, g/L	138.0 (127.0–151.0)
International normalized ratio	1.02 (0.97–1.09)
Albumin, g/L	41.4 (38.3–43.8)
Alanine aminotransferase, U/L	21.1 (15.0–33.0)
Aspartate aminotransferase, U/L	25.0 (19.6–33.0)

Hao Am J Gastro 2020



Wang J Hepatol 2020

Case 6. Hepatitis in Pregnancy

- 24yo 33 wks gestation with nausea and vomiting and RUQ pain. Taking acetaminophen 1gm q6; has dog and bird; recent visit to mom in NC.
- T 37.2; BP 158/110;2/6 SEM; RUQ tender; no rash.
- Plt 103K; Hct 26; WBC 6.6 10%L; PMN 82%; G 85; creat 0.6; ALT 225; AST 559; TB 1.4; CRP 15.8; PT WNL; fibrinogen NL.

Case 4: Tired and jaundiced

- 27 year old male presents with fatigue and dark urine. Hx recent sexual exposures with other men.
- No fever, vitals normal. Mild icteric. ALT 1945 IU/ml; AST 1239 IU/ml; TB 4.2 mg/dl; WBC 3.2k nl diff.
- Total HAV pos; HAV IgM neg; HCV RNA neg; IgM anti-HBc pos; HBsAg pos; RPR neg; HIV 4th gen neg
- Ptr was tested and is HBsAg and anti-HBs neg

Question #4

Which is easiest to justify medically?

A. Repeat HBsAg and anti-HBs testing for partner
B. HBIG and HBV vaccine for partner
C. HBV vaccine for partner
D. Entecavir 0.5 mg/d for patient
E. TAF for partner

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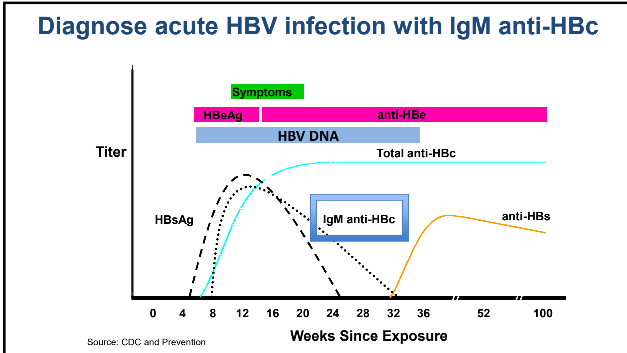
Diagnose acute HBV infection with IgM anti-HBc



2. No treatment indicated for acute HBV (unless fulminant)

3. Prevention by vaccine +/ HBIG

- HBsAg and anti-HBs screening of partners
- Tools: HBIG and/or HBV vaccine (USA)
  - Engerix, Recombivax, Heplisav-B, Pediarix, Twinrix
- Post-exposure:
  - Vaccinated and anti-HBs >10 ever, done*
  - No hx vaccine and/or anti-HBs >10, HBIG and vaccinate

*may be exception for patients with immunosuppression like HIV or dialysis

Schillie MMWR 2018

3. Prevention by vaccine +/ HBIG con't

- Pre-exposure:
  - no vaccine hx – vaccinate
  - Vaccine hx no testing – test for anti-HBs, boost or revaccinate if neg, retest anti-HBs

MMWR 2018

Acute hepatitis in HIV

46 y/o HIV pos male, CD4+ lymphocyte 235/ml³, HIV RNA undetect; HBsAg pos; no symptoms on TDF/FTC/RAL. Liver enzymes increased from ALT of 46 to 1041 IU/L. TB was 2.3. He has a long history of various ART regimens. He is sexually active with other men.

Acute hepatitis in HIV

Which of the following is the most likely cause of hepatitis:

A. toxicity from the RAL
B. acute HCV infection
C. IRIS
D. resistant HBV
E. HDV

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Recognize acute HCV in HIV POS MSM

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 60 / No. 28 July 22, 2011

World Hepatitis Day — July 28, 2011

July 28, 2011, marks the first official World Hepatitis Day established by the World Health Organization

Sexual Transmission of Hepatitis C Virus Among HIV-Infected Men Who Have Sex with Men — New York City, 2005–2010

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