8 – Acute Hepatitis

Speaker: David Thomas, MD

Acute Hepatitis

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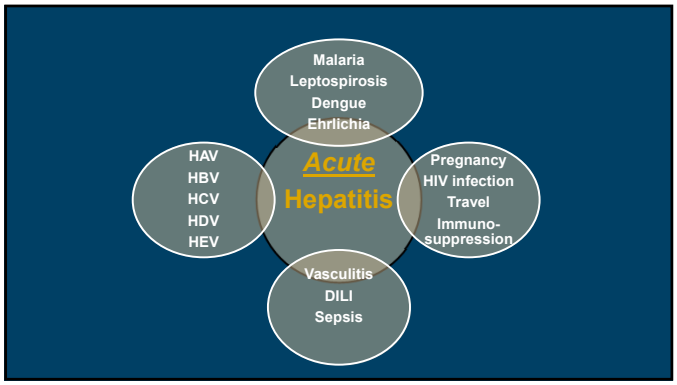
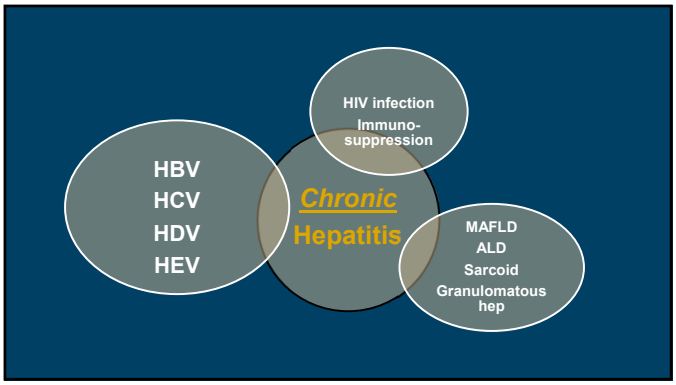
7/1/2024

Disclosures of Financial Relationships with Relevant Commercial Interests

- Data and Safety Monitoring Board: Merck
- Advisory Board: Merck, Excision Bio





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

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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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The cause of his illness is:

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Courtesy E Prochaska, MD

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 (ALT) and muscle (CPK): lepto, flu, adeno, EBV, HIV, malaria, Rickettsia/Ehrlichiosis, tularemia, TSS, coxsackie, vasculitis

Leptospirosis

4. Diagnosis:
   - PCR most useful (urine pos longer)
   - serology late

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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.

Acute hepatitis in Uganda

PREVIEW QUESTION

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

Acute hepatitis in Uganda

PREVIEW QUESTION

Which test result is most likely positive?

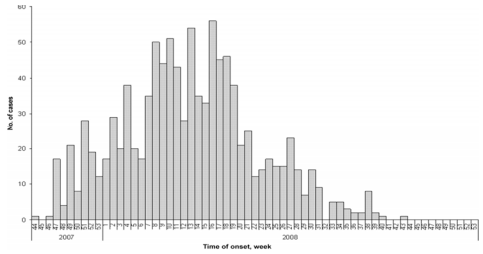
A. Ebola PCR
B. IgM anti-HEV *
C. IgM anti-HAV
D. Schistosomiasis "liver" antigen
E. 16S RNA for Rickettsial organism

1. Vaccination works to prevent hepatitis A *up to 14d after* exposure in healthy young adults

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; Al-Shimari BMC Public Health 2023

3. Hepatitis E: Epidemiologic Clues

–Outbreaks – contaminated water in Asia/Africa

–Sporadic - undercooked meat (BOAR, deer, etc)

–USA: endemic rare, genotype 3, IgG serology positive far more than can be explained by cases - can be hard to interpret

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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

–Vaccine: not USA (not boards)

PREVIEW QUESTION

Acute Hepatitis at ID Week

- 42 year old homeless male approaches a group of ID fellows 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

PREVIEW QUESTION

Fellow worried about what?

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

Acute hepatitis at ID week

PREVIEW QUESTION

Fellow worried about?

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

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

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

Morbidity and Mortality Weekly Report (*MMWR*)

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

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

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

Case Count as of December 13, 2016

Outbreak of hepatitis A in Hawaii linked to raw scallops

Outbreak

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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: All children 1-18 yrs receive hepatitis A vaccine (since 2006)
  - HIV, HCV or HBV positive persons/chronic liver disease/homeless/MSM/PWID/Travelers/adoptee exposure
- *Post-exposure:* vaccinate or possibly IG if
  - > 40 years or immunosuppressed then IG is 'preferred'

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)

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 (antibodies for routine screen)

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

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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 in a pilot

What agent caused this illness?

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B. Hepatitis A
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Hepatitis with bacterial infections

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

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 always WRONG answers

8 – Acute Hepatitis

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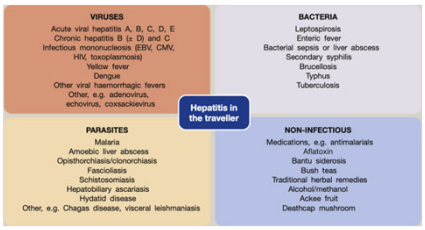
Hepatitis with travel to developing country

There is a broad differential



Jones Medicine 2017

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

Hepatitis in pregnancy

What is the best diagnosis?

A. HELLP
B. Acute fatty liver of pregnancy
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Allen OB GYN 2005

Hepatitis in pregnancy

1. Rule out HSV
   ~50% have muco-cutaneous lesions
   High mortality without acyclovir

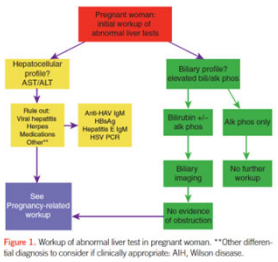

Figure 1. Workup of abnormal liver test in pregnant woman. **Other differential diagnosis to consider if clinically appropriate: AIH, Wilson disease.

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)

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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

Fulminant Hepatitis

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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
- Low plt: Ehrlichial or rickettsial
- Find the lepto case (jaundice>hepatitis)

Thanks and good luck on the test!

Questions:

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