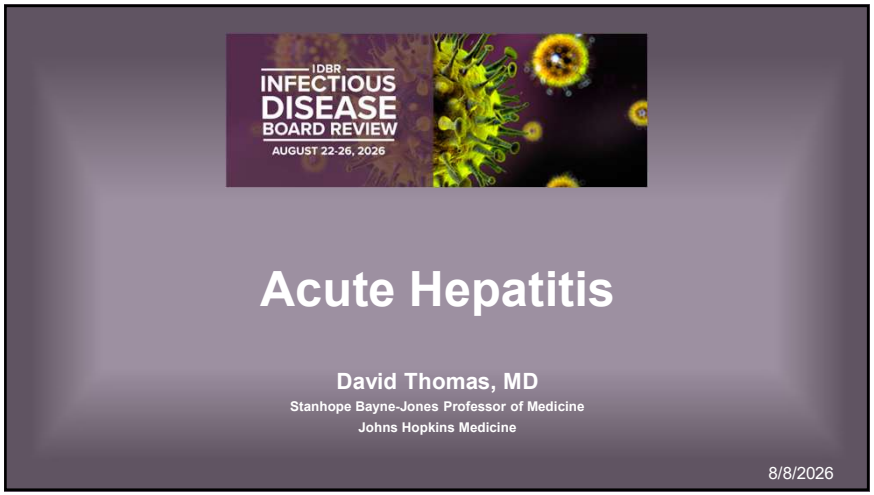

Acute Hepatitis

David Thomas, MD
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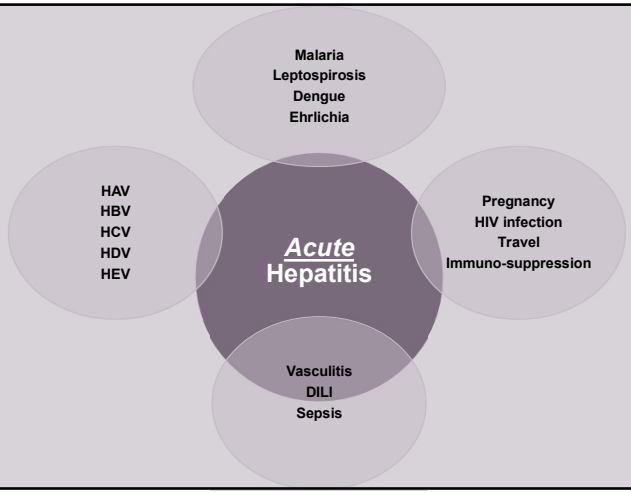
8/8/2026

Disclosures of Financial Relationships with Relevant Commercial Interests

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



Question #1

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

Courtesy E. Prochaska, MD

Question #1

- 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

Question #1

What is the cause of his illness?

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

Courtesy E. Prochaska, MD

Leptospirosis

1. Exposure to fresh water (e.g., 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

Question #2

Acute Hepatitis in Pakistan

- 52-year-old male has malaise, jaundice and RUQ pain
- One month ago, he returned from 1 month visit with family in NW Pakistan. Typical family exposures in village. No known bites. Mostly inside due to rain. No alcohol or sexual exposures
- Grew up in Pakistan until 24 yrs; unsure about vaccinations.
- On losartan for HTN and metformin for diabetes
- T 100.2 F; jaundiced; RUQ tender. ALT 1245 IU/ml; TB 3.2 mg/dl; WBC 3.2k nl differential; HIV neg

Courtesy E. Prochaska, MD

Question #2

Which test result is most likely positive?

A. Andes virus PCR
B. IgM anti-HEV
C. IgM anti-HAV
D. Schistosomiasis “liver” antigen
E. 16S RNA for Rickettsial organism

Prior HAV Infection/Protection is Near Universal in Persons Residing in LMIC

HAV Seroprevalence by Age in 2005

Age Group	Southeast Asia	East sub-Saharan Africa	High-income North America
1-4	20	98	0
5-9	35	100	0
10-14	35	100	5
15-19	56	100	11
20-24	67	100	16
25-34	79	100	22
35-44	88	100	29
45-54	96	100	37
55-64	100	100	47
65-74	100	100	56
75-84	100	100	68
85+	100	100	79

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Jacobsen Vaccine 2010

Acute Hepatitis E
Epidemiologic Clues

- Outbreaks: contaminated water and flooding in SE 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

Acute Hepatitis E
Clinical Clues

- Fatalities in pregnant women
- GBS and neurologic manifestations (vs other hep viruses); pancreatitis
- Diagnosis: RNA PCR; IgM anti-HEV
- Treatment: ribavirin for chronic
- Vaccine in China

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?

Question #3

With what diagnosis was the fellow most concerned?

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

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]

[1]Epidemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta, Georgia; [2]County of San Diego Health and Human Services Agency, and [3]Division of Global Migration and Quarantine, Centers for Disease Control and Prevention, San Diego, California; and Divisions of [4]Foodborne, Waterborne, and Environmental Diseases, and [5]Viral Hepatitis, Centers for Disease Control and Prevention, Atlanta, Georgia

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

Hepatitis A: Key Epidemiologic Clues: People, Places and Foods

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HEALTH • 5 MIN READ

There is a hepatitis A outbreak in LA County. Why you need to know

UPDATED MAY 15, 2025

By Katia Hetter

Hepatitis A: Key Epidemiologic Clues: People, Places and Foods

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

Case Count as of December 13, 2016

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.

Hepatitis A: Key Clinical Clues

- Clinical syndrome
  - Fulminant on HCV
  - Relapsing: symptoms/jaundice recur <12 mo

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

Vaccination Works to Prevent Hepatitis A
Up to 14 Days 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)

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Victor NEJM 2007

Acute Viral Hepatitis B Clues

- Most linked to sex, drugs
  - Nosocomial (finger stick 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)

Prevention by Vaccine +/ HBIG

- Pre-exposure:
  - HBV vaccine (Engerix, Recombivax, Heplisav-B, Pediarix, Twinrix)
- Post-exposure:
  - Vaccinated and anti-HBs >10 ever, done*
  - No history of vaccine and/or anti-HBs <10IU, HBIG and vaccinate
  - Infant: birth dose vaccine, HBIG, maternal TDF**

*May be exception for patients with immunosuppression like HIV or dialysis;**TDF if maternal HBV DNA >200,000 IU/ml

Schillie MMWR 2018

Acute Viral Hepatitis Delta Will Be with HBV

- HDV
  - HBV co-infection
    - 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

Question #4

Hepatitis and Confusion After Camping

- 65 y/o with T2DM, HTN and memory impairment presents with acute confusion and cough
- 1 week PTA: lethargy and confusion during camping that progressed until found 'down' and incontinent
- Avid outdoors; lives and camps in rural PA; frequent tick and mosquito bites, SP doxy x1 one month earlier; no animals
- T 37.1, 95% on 3L; oriented x2; no rash; RUQ tender

Courtesy Jillian Peters

Question #4

	OSH Presentation	JHH ICU
WBC	12.4	11.4
Hemoglobin	10.6	8.0
Platelets	116	42
Na	132	142
Cr	5.4	3.0
AST	6590	564
ALT	3646	671
Alk Phos	83	228
T. Bili	1.3	9.0
Lactate	9.3	6.8
Ammonia	260	82

- INR 1.6
- APTT 45.6
- D-dimer >30
- Fibrinogen 110
- LDH 1390
- Ferritin: 25,299
- CK 14,000
- Chest CT: bilat UL consolidation

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Courtesy Jillian Peters

Question #4

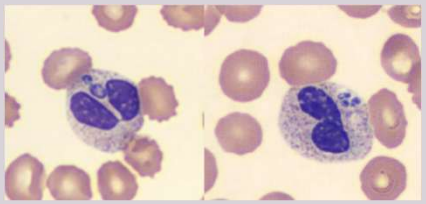
What agent caused this illness?

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

Hepatitis and Confusion After Camping

A.Phagocytophilum,DNA,PCR **DETECTED !**
Comment: REFERENCE RANGE: NOT DETECTED

A.Phagocytophilum Ab IgG <1:64	1:64 ^
A.Phagocytophilum Ab Interp.	SEE BELOW
Comment: Equivocal: Due to a low/negative IgG and a positive IgM, the presence of a recent/current infection should be confirmed by running acute and convalescent sera in parallel and an increasing IgG value detected.	
A.Phagocytophilum Ab IgM <1:20	1:160 ^
E.Chaffeensis Ab IgG <1:64	<1:64



Courtesy Jillian Peters

Hepatitis with Bacterial Infections

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

Hepatitis with Bacterial Infections

2. When more cholestatic but still with liver, lung, renal, skin, CNS disease consider coxiella burnetti and spirochetes (syphilis and lepto) vs. Rickettsia/Ehrlichia/Anaplasma

Hepatitis with Bacterial Infections

3. Hepatitis F or G are always WRONG answers

Question #5

Hepatitis in Pregnancy

- 37-year-old 35 weeks gestation with 1 week fever, chills, abd pain.
- Pre-term labor and healthy baby delivered C-section
- Rapid deterioration of mom: fever with severe myalgia and low BP
- Plt 143K; Hb 8.6; WBC 6.4K 20% bands; glucose, creat and INR WNL; ALT and AST >2000 IU/ml; BR nl; Fibrinogen NL

Courtesy V Fabre; Allen OB GYN 2005

Question #5

What is the best diagnosis?

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

Hepatitis in Pregnancy

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

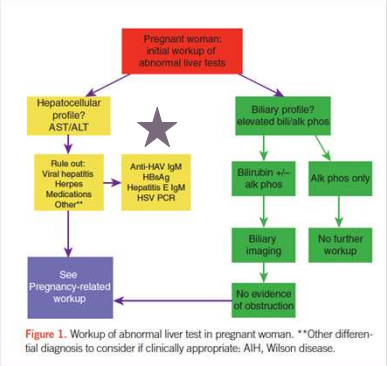


Figure 1. Workup of abnormal liver test in pregnant woman. **Other differential diagnosis to consider if clinically appropriate: AIH, Wilson disease.

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

ACOG 2016

Hepatitis in Pregnancy

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

3. AFLP – severe: Abn ALT and TB PLUS- low glucose, incr INR, low fibrinogen; elevated WBC (Swansea criteria)

Question #6

Fulminant Hepatitis

- 65-year-old man with Hx of jaundice
- 2 weeks before finished amoxicillin/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

Question #6

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

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

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

Acute Hepatitis Summary

- ★ • HEV: flood/travel or boar
- ★ • Acute A: vaccine effective
- ★ • HIV: acute HCV in MSM
- ★ • Low platelet: Ehrlichial, anaplasma or rickettsial
- ★ • Find the lepto case (jaundice>hepatitis)!

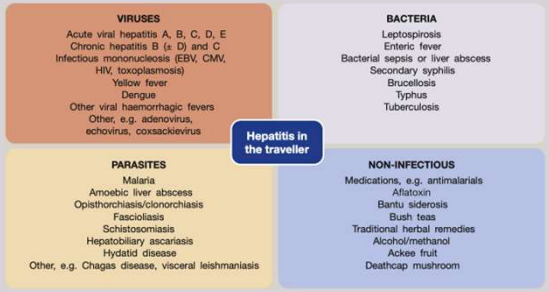
Thanks and good luck!

Questions?

Dave Thomas: dthomas@jhmi.edu

Hepatitis with Travel to Developing Country

There is a broad differential



Jones Medicine 2017