AMERICAN COLLEGE OF EMERGENCY PHYSICIANS
SCIENTIFIC ASSEMBLY
1999

The ABCs of Hepatitis

The many forms of hepatitis have been reclassified and renamed in recent years. The emergency physician must consider how to differentiate among them because the treatment and disposition of the patient, as well as prophylaxis of contact, may hinge on the etiology. In this course, the participants will learn the most current terminology and presentation of the infectious types of hepatitis. Diagnostic modalities currently available and appropriate emergency department management and follow-up will be discussed.

- Describe the pathogenic process and clinical presentation for each type of hepatitis.
- Discuss the emergency department management, including hospital admission criteria.
- Discuss the diagnostic studies of the greatest use to the emergency physician.
- Describe available treatments and the indications for prophylaxis.
- Discuss the ramifications of the legislation being discussed in Congress concerning hepatitis C.

TH-235
Thursday, October 14, 1999
12:00 PM - 12:55 PM
Room # N208
Las Vegas Convention Center

FACULTY

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1999 SCIENTIFIC ASSEMBLY

The ABC's of Hepatitis

Course # TH-235

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I. COURSE DESCRIPTION

This course will review the common causes of hepatitis with a specific focus on infectious etiologies. Diagnostic modalities, appropriate emergency department management, disposition and follow-up will be discussed. These points will be illustrated through case discussions.

II. OBJECTIVES

- **Identify clinical signs suggestive of early hepatitis**
- **Develop a differential for hepatitis**
- **Understand the role of the lab in screening, diagnosis and etiologic identification of hepatitis**
- **Identify patients requiring admission for hepatitis**
- **Describe available treatments and indications for prophylaxis**

III. COURSE OUTLINE

Viral Hepatitis
- Clinical Presentation
- Early identification of hepatitis
- Historical clues to raise your suspicion
- Risk Factors

Diagnosing Hepatitis
- Laboratory
- Imaging
- Lab interpretation suggesting viral hepatitis

Differential Diagnosis
- Infectious hepatitis
- Alcoholic Hepatitis
- Toxic Hepatitis
- Autoimmune
- Nonalcoholic Steatohepatitis

Viral hepatitis
- Hepatitis A
- Hepatitis B
- Hepatitis C
- Serologic tests

Treatment
Prophylaxis
Public health issues

The clinical challenge

Case 1: 52 year old with malaise, abdominal pain and vomiting
Case 2: 38 y.o. jaundiced male, hx of drug and alcohol abuse

Who has hepatitis?
Both have hepatitis, however the former patient is more typical of the presentation seen in the ED. It is this subtle presentation that is frequently misdiagnosed, usual as a viral gastroenteritis. The clinical challenge is to identify these patients early in the course of their illness to make a difference in subsequent morbidity and reduce the public health impact.
What is the cause?
Once the diagnosis of hepatitis has been made, the next challenge is to identify the etiology. The cause has important treatment and public health implications.

Hepatitis

- Generic term referring to inflammation of the liver
- Most common liver disease encountered by the EP

Etiology
Infectious
- Viral
- Pyogenic or amebic

Non-infectious
- Toxin
- Auto-immune
- Nonalcoholic Steatohepatitis (NASH)

Viral Hepatitis

Epidemiology
- About 50,000 reported cases per year
- 47% hepatitis A
- 34% hepatitis B
- 16% hepatitis C
- 3% unspecified
- CDC estimates 500-750,000 actual new cases
- 15,000 deaths per year
- 4,000,000 carriers

Clinical Presentation

- polymorphic presentation
- range from asymptomatic to fulminant hepatic failure
- generally 4 phases described

Phase 1: asymptomatic
- viral replication
- serologic and enzyme markers positive
- patient unaware of disease process

Phase 2: prodromal
- nausea, vomiting
- malaise
- anorexia
- arthralgia
- altered taste
- puritis

Phase 3: icteric
- increased GI symptoms
- RUQ pain
- hepatomegaly
- dark urine, light stool

Phase 4: convalescent
- symptoms resolve
- icterus clears
- LFT's normalize or infection becomes chronic

Early identification of hepatitis

"Jaundice is the disease your friends diagnose" – Osler
Pre-icteric hepatitis is the diagnosis we miss. By paying attention to historical clues and asking about risk factors we can heighten our suspicion of hepatitis in the non-specific gastroenteritis.

Historical clues to raise your suspicion
- Antecedent fatigue
- Anorexia and weight loss
- Dark urine, pale stool

- Aversion to smoke and strong odors
- Polyarthralgias
- Pruritis

Risk Factors
Fecal-oral
Poor sanitation, institutionalized, travel, food or waterborne outbreaks
Blood-borne
Homosexual or heterosexual with multiple partners, parenteral, occupational (health care)
Immunocompromised
HIV infection, hemodialysis, immunosupressants
Toxins
Medications, alcohol, industrial exposure, alternative medications

Diagnosing Hepatitis

- Need to consider in the differential
- Easy if jaundiced or the labs are ordered
- Not cost effective to order on all non-icteric "viral syndromes"
- Imaging rarely helpful

Laboratory: ***So what should you order?***
Viral syndrome but positive historical features or risk factors:
- ALT (alanine aminotransferase)
- Urine dip for bilirubin

Icteric or ALT,urine dip positive
- ALT, AST
- Bilirubin, total and direct
- Alkaline phosphatase, LDH
- Lipase
- Prothrombin time (PT)

Imaging
- Are rarely indicated or helpful in acute hepatitis
- Ultrasound may be useful in atypical presentations to identify ductal disease, gallbladder abnormalities or abscess

Lab interpretation suggesting viral hepatitis:
- 10 to 100 fold increase in aminotransferases
- ALT > AST
- bilirubin is usually moderately elevated (5-10 mg/dl)
- direct:indirect in equal proportions
- alkaline phosphatase and LDH maybe elevated but rarely more than 2-3 times normal
- elevated PT suggests a complicated course
- WBC is not useful

<u>Differential Diagnosis</u>

- The differential diagnosis varies with the stage of presentation
- Once hepatitis has been identified, the cause must be determined
- Causes are generally infectious vs. non-infectious
- Infectious causes are usually viral but non-viral infectious hepatitis can occur

Infectious

Viral	**Non-Viral**
Hepatitis A	Gram– rods (adults)
Hepatitis B	Gram+ cocci (children)
Hepatitis C	N. Gonorrhoeae
Hepatitis E	C. Trachomatitis
Hepatitis non-ABCDE	Syphylis
HGV	Entamoeba histolytica
EBV	Legionellosis
CMV	Salmonellosis
Varicella-zoster	Tularemia
HSV	Leptospirosis
Adenovirus	Q-fever
HIV	Toxoplasmosis
	Brucellosis

Alcoholic Hepatitis

- clinical spectrum from mild N&V and abdominal pain to liver failure
- acute onset, slow to resolve
- mortality 20 -60 % in admitted patients
- may have hepatomegaly from fatty infiltrates to a small liver from cirrhosis
- the differential is broad since other ethanol induced diseases are often present concurrently

Laboratory values suggesting alcoholic hepatitis:
- AST>ALT (1.5:1)
- Moderate elevation of transaminases (5-10X normal)
- Bilirubin is variable
- Alkaline phosphatase usually normal

Toxic Hepatitis

Cholestatic
- painless jaundice, elevated direct bilirubin
- alkaline phosphatase > 3X normal
- ultrasound often needed to distinguish from biliary causes

Cytotoxic
- presents like acute viral hepatitis
- can progress to fulminant hepatitis and cirrhosis

Drug-induced Hepatitis

Cytotoxic	**Cholestasis**
Acetominophen	Anabolic steroids
Amiodarone	Oral contraceptive agents
Amphotericin	Erythromycin
Isoniazid	Lovastatin
Ketoconazole	Haloperidol
Penytoin	Phenobarbital
Salicylate	Verapamil
Valproic acid	

Viral hepatitis: The ABC's

Hepatitis A

Epidemiology

- 30,000 cases reported annually but actual cases estimated to be 125,000 to 500,000 in US
- incidence cyclical
- most cases are pediatric
- high risk: travelers, day-care, raw shellfish, institutionalized, crowding
- up to 50% of adults in the US have serologic evidence of HAV exposure

Pathophysiology

- fecal-oral spread
- viral shedding occurs 2-3 weeks before symptoms and persists for 2 weeks (up to 10 in infants)
- no carrier or chronic hepatitis state
- fulminant hepatitis is rare but can occur

Presentation

- most cases are mild, anicteric, undiagnosed
- often presents as gastroenteritis or a viral RTI
- most common in children, jaundiced <10%
- adults have a more severe course, 70-80% icteric
- signs may also include fever, hepatomegaly, dark urine
- anorexia, N&V, fever and rash more common than with hep B or C

Hepatitis B

Epidemiology

- estimated 50-250,000 new cases per year in US
- 1 million chronic carriers
- 5,000 deaths per year from chronic liver disease
- high risk: IVDA, male homosexuals, chronic dialysis, health care workers with blood exposure

Pathophysiology

- transmitted 3 ways: parenterally, sexual contact, mother to infant
- incubation period about 75 days

Presentation

- most cases mild to moderate, anicteric
- 90% of pediatric cases are asymptomatic
- course more insidious in onset and prolonged than hepatitis A
- 10% preceded by a "serum-sickness-like" illness
- 90% completely recover, 1-3% develop fulminant hepatitis

Hepatitis C

Epidemiology

- post-transfusion hepatitis prior to available screening methods
- now mainly in IV drug abusers, 2/3's are positive in 2 years of use
- 4,000,000 carriers
- 10,000 deaths/yr

Pathophysiology

- transmitted 3 ways: parenterally, sexual contact, mother to infant
- incubation period about 50 days but extremely variable
- 85% go on to chronic hepatitis
- 20% develop cirrhosis

Presentation

- 80% of cases anicteric and asymptomatic
- rarely develop fulminant hepatitis

Risk Factors Associated with Transmission of HCV

- Transfusion or transplant from infected donor
- Injecting drug use
- Hemodialysis (yrs on treatment)
- Accidental injuries with needles/sharps
- Sexual/household exposure to anti-HCV-positive contact
- Multiple sex partners
- Birth to HCV-infected mother

Other viruses

- HGV, unclear of clinical significance
- HEV, likeHAV, rare in US
- mild hepatitis associated with childhood systemic viruses
- EBV, CMV, HSV, Varicella
- can be severe in immunocompromised

So which is it?

- Difficult to distinguish between viral etiologies clinically
- Risk factors may be suggestive
- Serology, although not immediately available is important to send for prognostic and public health reasons

<u>Viral hepatitis: Serologic tests</u>

- Multiple serologies are available and the rationale is often confusing
- Ideally your department should have a standardized "viral hepatitis screen"
- Viral hepatitis screen usually consists of 4 tests:

IgM anti-HAV
IgM anti-HBc
HBsAg
anti-HCV

Treatment of Acute Hepatitis

- primarily supportive
- hydration
- ensure caloric intake
- treat complications
- antibiotics generally not useful, may be beneficial in fulminant
- corticosteroids may make it worse
- interferon not helpful in acute hepatitis probably helpful in chronic hepatitis B or C
- drugs with hepatotoxic potential should be discontinued

Prophylaxis

- viral hepatitis is a reportable disease
- immunoprophylaxis should be offered to close personal contacts
- prophylaxis varies with viral cause but may consider gamma-globulin pending serologic determination

Disposition

- admission rarely necessary
- education regarding disease process
- food handlers with HAV should not work while infective
- children with HAV may return after other children immunized

Indications for admission

- signs of encephalopathy: agitation, altered sleep pattern, personality change, altered mental status
- severe dehydration
- intractable vomiting
- age greater than 50
- severe underlying disease
- immunosuppression
- PT prolonged > 3 seconds
- hypoglycemia
- electrolyte disturbance
- bilirubin > 20

Public health issues

Health Care Providers

- Seropositivity of HBV 30% in ED nurses and 15% in ED physicians
- 30 year risk for physicians is 1 in 13
- 30 year risk of death is 1 in 540
- 18% of inner city ED patients HCV positive

Prophylaxis

- all health care providers should get HBV immunization
- protective antibody present in 95% after 3 vaccine series
- up to 60% lose immunity in 7-10 years
- HBIG reduces risk by 75% in acute exposure
- should be given in 24 hours of exposure but can be effective even within 2 weeks
- HBIG recommended post HCV exposure but unknown benefit

HBIG in Acute Occupational Exposure
Unvaccinated – one dose as soon as possible, (0.06mL/kg IM)
Vaccinated – unknown or low titers, one dose asap

HAV

Routine Childhood Hepatitis A Vaccination
Unresolved issues/considerations:

- immunogenicity in infants
- development of combination vaccines
- duration of protection
- cost-effectiveness

ACIP Recommendations - Hepatitis A Vaccine: Preexposure
Persons at increased risk for infection:

- travelers to intermediate and high HAV-endemic countries
- homosexual and bisexual men
- drug users
- persons with chronic liver disease
- Communities with high rates of hepatitis A (e.g., Alaska Natives, American Indians)
- routine childhood vaccination

Control of Community-wide Outbreaks
- Dependent upon the type and extent of the outbreak
- Contact your public health department

Postvaccination Testing
- Not recommended because of the high response rate among vaccinees
- No commercially available test to measure vaccine response

Hepatitis A Prevention - Immune Globulin
Preexposure:
- travelers to intermediate and high HAV-endemic regions

Postexposure (within 14 days):
- Routine
- Household and other intimate contacts
- Selected situations
- Institutions (e.g., day care centers)
- Common source exposure (e.g., food prepared by infected food handler)

HBV

Elimination of Hepatitis B Virus Transmission
- Prevent chronic HBV Infection
- Prevent chronic liver disease
- Prevent primary hepatocellular carcinoma
- Prevent acute symptomatic HBV infection
- Prevent perinatal HBV transmission

Recommended vaccination:
- Routine vaccination of all infants
- Vaccination of children in high-risk groups
- Vaccination of all unvaccinated children at 11-12 years of age
- "high-risk" adolescents at all ages
- Vaccination of adults in high-risk groups

Breaking news
- Thimersol free (preservative) hepatitis B vaccine available
- FDA approval on August 27, 1999
- Distribution was to begin last month
- HBV treatment
- Interferon: about a third respond but almost all relapse
- Lamivudine is new antiviral now approved for use

HCV

Treatment of HCV: Interferon
- Some may benefit from interferon
- Usually relapses after drug stopped
- Poorly tolerated
- Probably no benefit in mild or advanced cases
- Need liver biopsy to decide
- Interferon + ribavirin shows promise for more sustained response
- Response after 1 year: 36% with combination therapy, 16% interferon alone

Other therapy
- No vaccine
- Unlikely to find one due to the various genotypes
- Protease inhibitors show promise
- 170,000,000 potential customers provide incentive to find therapies

Prevention of Hepatitis C
- Screening of blood, organ, tissue donors
- High-risk behavior modification
- Blood and body fluid precautions

Postexposure Prophylaxis for Hepatitis C
- No protective antibody response identified
- IG prepared from high anti-HCV titer plasma did not prevent infection in chimpanzees
- (ACIP) Revised Recommendation, February 1994:

"Recent studies indicate that IG does not protect against infection with HCV. Thus, available data do not support the use of IG for postexposure prophylaxis of hepatitis C. There are no data on the efficacy of IG for postexposure prophylaxis of other (non-HCV) parenterally-transmitted non-A, non-B hepatitis."

Recommendations
- Abstain from alcohol
- Obtain treatment for drug addiction
- Safe sex if multiple partners
- Do not share razors, toothbrushes
- Testing of sexual partners

HCV: Hot topic

- Increased public awareness
- More press, headlines
- "Targeted lookback", general notification and public education campaign announced January, 1998 by Department of Health and Human Services
- Plan to identify recipients of blood between 1988-92 from donors that later tested positive (after 1992)
- Just now being implemented
- 3,000,000 Americans unaware that they have HBC
- Leading cause of liver transplant
- Estimated to cost $600,000,000/year from medical care and lost productivity
- CDC predicts death toll will triple in next decade eclipsing that of AIDS
- Now infects 4X as many people as HIV