Acute Hepatitis:
An Approach to Infectious and Other Causes

Mary Anne Cooper MSc, MD, MEd, FRCPC

Faculty/Presenter Disclosure Slide 1

- **Faculty:** Dr. Mary Anne Cooper
- **Relationships with commercial interests:**
  - **Consulting Fees:** Lupin Pharmaceuticals, Canada

Objectives

1. Develop a differential diagnosis of acute hepatitis
2. Consider the infectious etiologies of acute hepatitis
3. Review appropriate biochemical investigations for acute hepatitis
4. Develop a treatment plan for acute hepatitis

Acute Hepatitis

- Mr. A.O., 65 y.o.
- PMH: TIA, CAD, a. fib. (coumadin x 3 mo, metoprolol, amiodarone x 1 mo), hyperlipidemia (atorvastatin x 2 mo)
- 40 pack-year smoking hx, quit 8 yrs ago
- 3 alcoholic drinks per day x yrs

Acute Hepatitis

- 5 d prior - stopped coumadin, amiodarone
- 4 d prior - D/C cardioversion
  - Propafol, Versed; no complications reported
- 3 d prior - fever chills, N/V, malaise
- 1 d prior - T38.9^{o}C
  - Tylenol Plain x 2

Acute Hepatitis

- Day of presentation
  - FD - T40.0^{o}C; Tylenol plain x 2; sent to E.R.
  - T39.9^{o}C; Tylenol plain x 2
  - HR 80-120 bpm, a. fib.; no CHF, chest clear
  - Obese, no cutaneous stigmata liver disease
  - Liver edge 2 cm BCM = 12 cm span
  - No splenomegaly
  - No asterixis

Acute Hepatitis - Case Data

DATE	14										
AST	3639										
ALT	3078										
ALP	117										
Bili	24										
INR	1.41										
BUN	4.3										
Cr	87										

Acute Hepatitis

- Diagnosis
  - Hepatitis
  - Acute hepatitis

Acute Hepatitis

- Definitions
  - Acute hepatitis
    - < 26 wks
  - Severe acute hepatitis
    - < 26 wks, INR > 1.5
  - Fulminant hepatitis (or acute liver failure)
    - Severe acute hepatitis
    - Hepatic encephalopathy (HE)

Acute Hepatitis

- Infectious
- Toxin/drug
- Autoimmune
- Metabolic
- Thromboembolic

Acute Hepatitis

	Hepatocellular			Cholestatic		Infiltrative
	Ischaemia, AIH,Toxins	Viral	Alcohol	Complete	Partial	Infiltrative
AST&ALT	50-100x	5-50x	2-5x	1-5x	1-5x	1-3x
ALP	1-3x	1-3x	1-10x	2-20x	2-20x	1-20x
Bili	1-5x	1-30x	1-30x	1-30x	1-5x	1-5x
INR	Increased, no response to vit K			Responds to sc vit K		N
Albumin	Decreased if chronic			N	N	N
Platelets	Decreased if cirrhotic			N	N	N

O'Brien. Clinics in Liver Disease. 2009

Acute Hepatitis - Case Data

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Acute Hepatitis

- Infectious – Viral
  - HAV - FHF - immunocompromised, > 40 y.o., travel to endemic area, underlying liver disease [vaccinate if known chronic liver disease]
    - α-HAV-ab IgM
  - HBV - risk profile, acute, flare of chronic
    - HBs ag, α-HBc-ab IgM
    - HDV – co-infection risk > superinfection
      - Decreasing incidence
      - α-HDV-ab

Acute Hepatitis

- Infectious – Viral
  - HCV – acute infection mild, often not aware
    - risks
      - α-HCV-ab, HCV RNA [source, patient]
  - HEV – enteric, endemic areas; travel history
    - α-HEV-ab

Acute Hepatitis

- Infectious Hepatitis – Other
  - Herpesviridae
    - Epstein Barr Virus (EBV)
      - Monospot test
    - HSV I and II (IgM antibody)
    - Varicella zoster virus (VZV)
  - Cytomegalovirus (acute but ? fulminant)
      - CMV IgM, IgG (provincial lab)

Acute Hepatitis

- Infectious Hepatitis – Other
  - Adenovirus
    - Paediatrics, immunosuppressed
  - Hemorrhagic Fever Viruses
    - Dengue, lassa, ebola, yellow fever

Acute Hepatitis

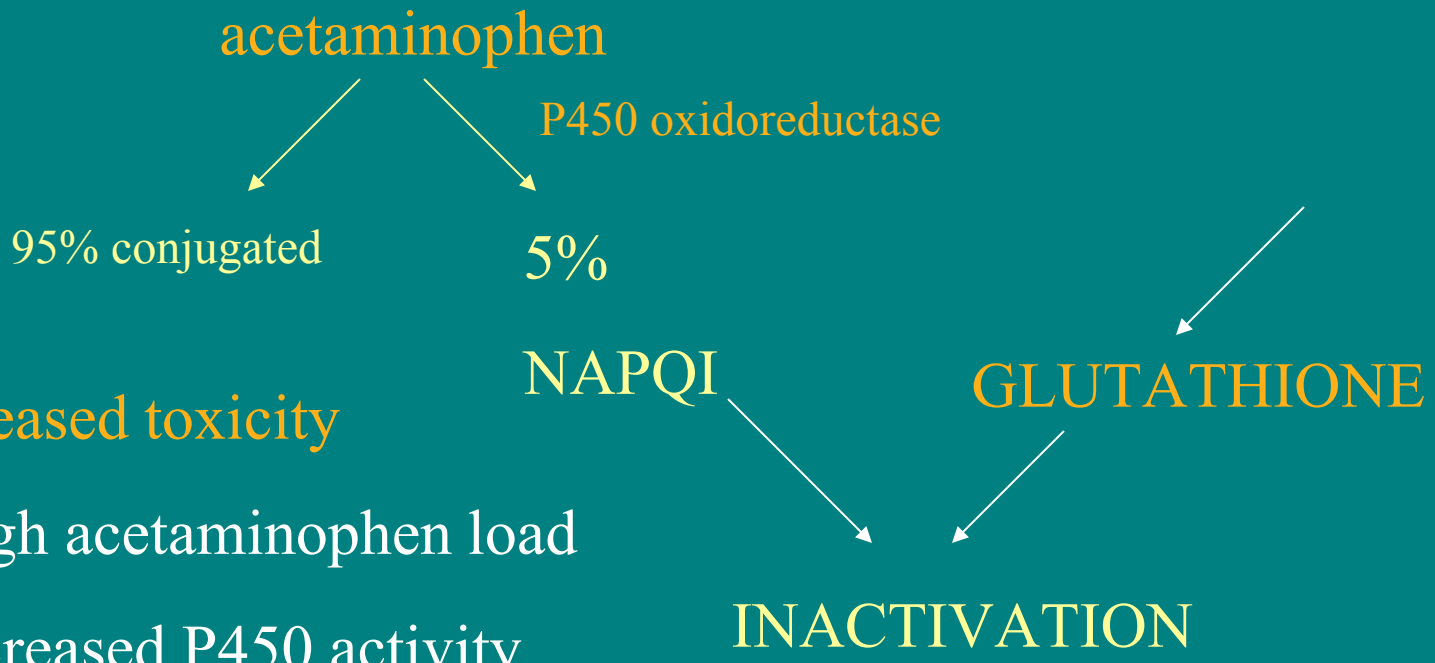
	A	B	C	D	E	CMV	EBV
Transmission	Fecal-oral	Parenteral, sexual	Parenteral	Parenteral	Fecal-oral		
Acute	+	+	(+)	+	+	+	+
Chronic	-	+	+	+	-	-	-
Fulminant	+	+	-	+	+	?	?
Test	IgM	c IgM	Ab, RNA	IgM	IgM	IgM	Monospot
Treatment of acute/fulminant	Support; OLT	Support; Lam, ETV; OLT	IFN	Support; Lam, ETV; OLT	Support; ? Riba; OLT	Support	Support

Acute Hepatitis

- Drugs/Toxins
  - Alcohol - chronic consumption
    - Maximum transaminase levels – about 300
    - If higher than this, look for other causes
  - Acetaminophen

Acute Hepatitis

- Drugs/Toxins



Increased toxicity

- High acetaminophen load
- Increased P450 activity
- Reduced glutathione stores

Acute Hepatitis

- Drugs/Toxins
  - Treatment of acetaminophen toxicity
  - N-acetylcysteine = NAC (Mucomyst)
    - Glutathione repletion
    - Best if < 8 hrs post ingestion
    - Some benefit up to 36 hrs
    - 140 mg/kg, then 70 mg/kg q4h for 72 hrs

Acute Hepatitis

- Drugs/Toxins
  - Amiodarone - 5-55% elevated AST/ALT
    - Insidious, asymptomatic
  - Atorvastatin - "statins" - 1-5% elevated AST/ALT
    - Cases of severe hepatitis with atorvastatin
    - [No increased risk in fatty liver]
  - Isoniazid, valproic acid, tetracycline
  - Amanita toxin

Acute Hepatitis

- Autoimmune
  - AIH, PBC, PSC, overlap
  - AIH – may have underlying chronic disease even if first ‘presentation’
    - ANA
    - Anti-smooth muscle antibody

Acute Hepatitis

- Cardiovascular/Thromboemolic
  - "shock liver"
  - Budd-Chiari
  - U/S with Dopplers
- Metabolic
  - Pregnancy - AFLP, HELLP
  - Wilson's - < 35-40 yrs (? maybe older)
    - Hemolysis, unconjugated bili
    - ceruloplasmin

Acute Hepatitis

- Mr. A.O.
  - Acetaminophen, background of chronic alcohol consumption
  - Atorvastatin, amiodarone
  - Viral
  - Shock - not documented during cardioversion

Acute Hepatitis - Investigations

- Acetaminophen level
  - Pitfalls?
- α-HAV-ab IgM
- HBs ag
- α-HBc-ab IgM
- ANA, ASMA
- Abdo U/S with Dopplers (but on coumadin)

Acute Hepatitis - Management

- Close monitoring - bleeding, edema, encephalopathy
- Frequent blood work
  - Liver profile, INR BID; CBC, lytes, BUN, Cr
- NAC - 140 mg/kg p.o. then 70 mg/kg p.o. q4h
- Vitamin K

Acute Hepatitis - Case Data

DATE	14	15-am	15-pm	16-am							
AST	3639	9170	13620	13700							
ALT	3078	6550	9680	10445							
ALP	117	146	167	180							
Bili	24	38	60	112							
INR	1.41	1.98	2.4	3.14							
BUN	4.3			9.4							
Cr	87			246							

Acute Hepatitis - Case Data

DATE	14	15-am	15-pm	16-am	16-pm	17-am					
AST	3639	9170	13620	13700	6645	2563					
ALT	3078	6550	9680	10445	6975	4337					
ALP	117	146	167	180	161	128					
Bili	24	38	60	112	141	158					
INR	1.41	1.98	2.4	3.14	2.12	3.0					
BUN	4.3			9.4	9.8	10.7					
Cr	87			246	331	420					

Acute Hepatitis

- Diagnosis?
- + α-HAV-ab IgM

Acute Hepatitis - Case Data

DATE	14	15-am	15-pm	16-am	16-pm	17-am	17-pm	19	24	28	
AST	3639	9170	13620	13700	6645	2563	1245	159	72	60	
ALT	3078	6550	9680	10445	6975	4337	3325	1260	247	90	
ALP	117	146	167	180	161	128	127	119	130	120	
Bili	24	38	60	112	141	158	163	195	338	285	
INR	1.41	1.98	2.4	3.14	2.12	3.0	3.03	1.79	1.55	1.51	
BUN	4.3			9.4	9.8	10.7	11.7	15.9	19.9	12.7	
Cr	87			246	331	420	435	528	387		

Acute Hepatitis - Summary

- Acute hepatitis
  - Consider all etiologies - hx, exam
  - Know which tests to order
  - Supportive care, monitor closely
  - NAC - low threshold to use