Hepatitis A
and
Hepatitis E

Luis S. Marsano, MD
Professor of Medicine
Division of Gastroenterology, Hepatology & Nutrition
University of Louisville and Louisville VAMC
2011

Viruses that cause Hepatitis in Humans

- Hepatitis A
- Hepatitis B
- Hepatitis C
- Hepatitis D
- Hepatitis E
- Coxsackie
- Echovirus
- Yellow fever
- Rubella
- Junin virus (Argentina)
- Machupo virus (Bolivia)
- Lassa virus
- Rift Valley virus
- Marburg virus
- Ebola virus
- Measles virus
- Human adenovirus
- CMV
- EBV
- HSV
- Varicella-Zoster

Hepatitis A

Hepatitis A

- Hepatovirus from Picornavirus family.
- 27-32 nm, linear, (+) sense, simple stranded RNA.
- Reservoir: human only
- Acquisition: fecal-oral; concentrated in oysters. Contaminated water or food, men having sex with men, blood during short viremic phase.
- Non-cytopatic; immune mediated injury by lymphocytes

Groups at Risk for HAV

- Healthy persons who travel to endemic areas,
- Workers in occupations with high likelihood of exposure,
- Family members of infected patients,
- Persons who adopt infants or children from endemic areas,
- Men who have sex with men,
- Persons who have tested positive for human immunodeficiency virus,
- Persons with chronic liver disease,
- Persons with clotting factor disorders,
- Users of injection and noninjection illicit drugs.

Hepatitis A
Sero-Prevalence

- ***Poor sanitation countries***:
  - near 100 % by age 5.
- ***Good sanitation countries (USA)*** :
  - 10 % by age 14;
  - 37 % in adults.

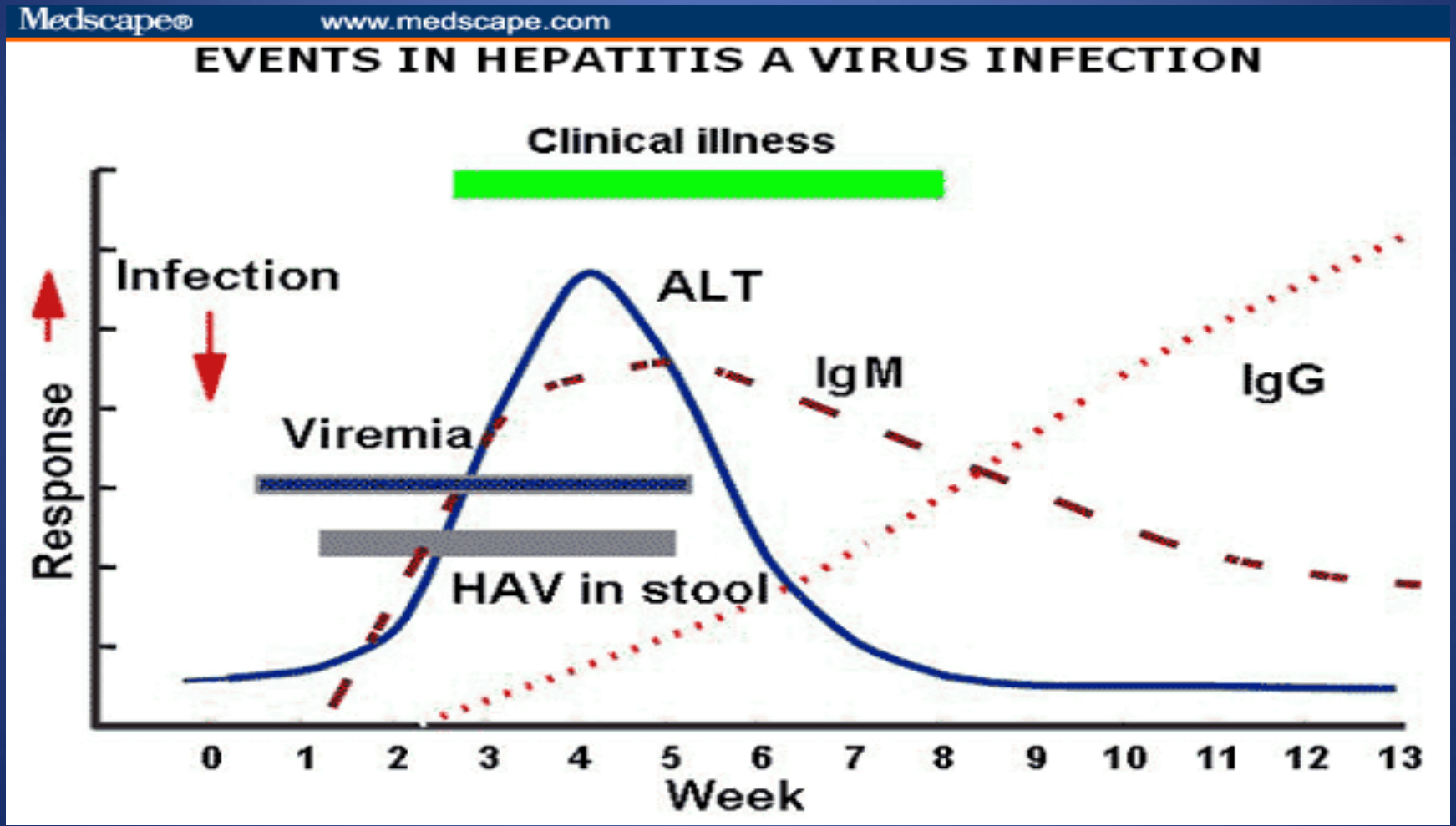
Hepatitis A
Clinical Features

- **Incubation**: 2-4 (up to 6) weeks
- Children < 2 year: 80% anicteric & asymptomatic
- Children > 2 y and adults: 80% icteric & symptomatic
- **Symptoms**: Fatigue (90%), anorexia (85%), jaundice (80%), nausea (75%), low fever (65%), headache, abdominal pain and myalgias.
- **Duration**: usually < 8 weeks

Hepatitis A
Atypical Manifestations

- **Relapsing hepatitis**: less than 10%; 2 or more bouts of elevated enzymes.
- **Cholestatic hepatitis**: Severe and prolonged jaundice > 10 weeks. Is rare.
- **Fulminant Hepatitis**: very rare but lethal in 50%. Increased risk in elderly and persons with chronic liver disease and HIV infection.
- **Auto immune hepatitis Type I:** after acute HAV in genetically predisposed.
- Mortality: Not increased by pregnancy.
  - a) younger than 49 = 0.3%;
  - b) older than 49 = 1.8%.

Sequence of Events in Acute HAV



Extra hepatic Manifestations of HAV

- Evanescent rash (14%)
- Arthralgia (11%)
- Leukocytoclastic vasculitis (legs and buttocks)
- Glomerulonephritis
- Arthritis (lower extremities)
- Cryoglobulinemia.
- Toxic epidermal necrolysis.
- Myocarditis
- Acute kidney Injury.
- Optic neuritis
- Transverse myelitis.
- Polyneuritis.
- Cholecystitis.
- Thrombocytopenia,
- Aplastic anemia,
- Red-cell aplasia
- Hemolysis in G6DH deficiency
- Pancreatitis.

Hepatitis A Vaccination Recommendation

- Children in areas with rate >20/100000
- High risk: traveler to endemic area, men having sex with men, illegal drug users, person with clotting factor disorder, researcher working with HAV.
- Chronic liver disease: HBV, HCV
- During community outbreaks.
- **Immunogenicity:** > 70% within 2-4 weeks after 1st dose, and 94-99% after second dose.

Hepatitis A
Post-Exposure Management

- Post-exposure prophylaxis can be done:
  - with Intramuscular “Immune Serum Globulin” (ISG) within 14 days from exposure at 0.06 mL/kg (69-89% effective and lasting 12-20 weeks) or
  - with Inactivated Vaccine given also within 14 days post-exposure.
- Response to vaccine is less robust:
  - before age 1 (due to circulating maternal antibodies), and
  - after age 40.
- Inactivated Vaccine is the preferred approach from age 1 to 40.
- Immune serum globulin is preferred in all other groups unless contraindicated due to IgA deficiency or hypersensitivity to ISG.

Hepatitis E

Hepatitis E

- 27-30 nm non-enveloped, single-stranded, positive-sense RNA Hepevirus.
- There are 4-6 genotypes. Genotypes 1 & 2 only in humans. Is not cytopathic; injury is immune mediated.
  - 1: India, China, Pakistan;
  - 2: Mexico;
  - 3: USA, France, Japan.
  - 4: China, Japan
  - There is an avian and a rat HEV variant.
- Acquisition:
  - Waterborne, fecal-oral, by organ meat ingestion, or by contact with animals. In USA swine is a common source. Deer meat and shellfish may be the source.
  - Rare person-person (1.5% intra-familial). Rare materno-fetal and by transfusion.
  - Increased risk in homosexual men.

Features of HEV in Different Areas

	Highly Endemic Area	Nonendemic Area
Geographic Area	Tropical & Subtropical Asia, Africa, Central America	USA, Western Europe, Asia-Pacific.
Human Disease	Highly frequent sporadic and endemic cases	Infrequent sporadic cases
Reservoir	Primarily human; possible environmental	Zoonotic (pig, boar, deer)
Primary transmission route	Fecal-oral by contaminated water	Undercooked organ meat; contact with animals.
Affected Groups	Young and healthy.	Elderly with comorbidities.
Disease in Pregnancy	High frequency of severe disease (22% FHF)	Not reported.
Prevalent Genotypes	1,2, (4).	3, (4).
Chronic Infection	Not reported.	In immunosuppressed (g-3)

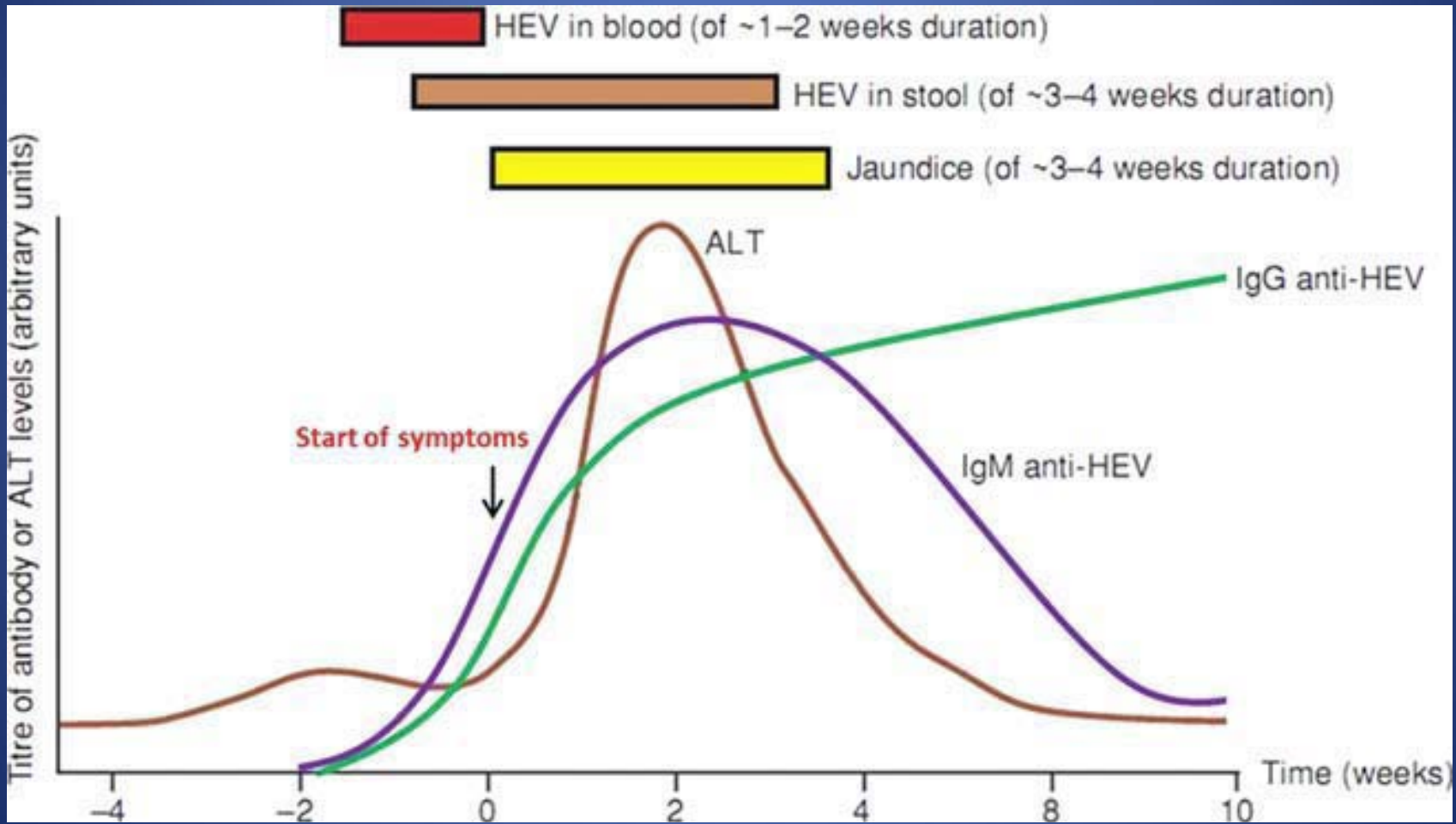
Hepatitis E

- **Types:** Sporadic, epidemic & endemic acute hepatitis. Rare chronic hepatitis.
  - **Sporadic:** traveler to endemic areas, pet owners, organ meat eaters, male homosexuals, military service (Midwest USA).
  - **Epidemic:** after heavy rain and flooding in areas with poor sanitation (India, China, Latin America, Africa)
  - **Endemic:** In areas were asymptomatic infection occurs at early age, like in Egypt
  - **Chronic hepatitis:** in immunosuppressed patients, with progressive liver damage an cirrhosis (worse with Tacrolimus than with CSA).
- **Reservoir: human**, pig, boar, sheep, cattle, rat,…
- **Prevention:** there is an experimental recombinant vaccine.

Hepatitis E

- **Incubation**: 2-10 weeks.
- **Prodrome**: 2 weeks of malaise, mild chills & fever, transitory macular rash.
- **Symptoms & Signs**: jaundice, nausea, vomiting, anorexia, aversion to food & smoking, abdominal pain, clay-color stool. Hepatomegaly in 65-80%; symptoms usually for 4 weeks.
- **Mortality**:
  - 0.1-0.6%; 15-25% during pregnancy in the epidemic form in India.
  - Mortality in pregnancy is low in Egypt and other endemic areas.
- **Diagnosis:**
  - Anti HEV-IgM last only 3-6 months, and is not always present in acute infection;
  - Anti-HEV IgG lasts for years;
  - HEV can be found by PCR in stool, serum, and bile.
- **Treatment:** Reduction in Immunosuppression is initial therapy**;** may need Peg-IFN and Ribavirin x 3-6 months in chronic HEV.

Sequence of Events in HEV



Extrahepatic Manifestations of HEV

- Acute Pancreatitis.
- Hematologic: thrombocytopenia, hemolysis.
- Henoch-Schonlein Purpura.
- Membranous Glomerulonephritis.
- Neurologic:
  - Guillian-Barre Syndrome
  - Meningoencephalitis.
  - Pseudotumor cerebri.
  - Cranial Nerve Palsy.
  - Bilateral Pyramidal Syndrome.
  - Peripheral Neuropathy.