### Virology

<table>
<thead>
<tr>
<th>Class</th>
<th>Flavivirus</th>
<th>RNA single strand</th>
<th>envelope</th>
<th>1988</th>
</tr>
</thead>
</table>

### Nucleocapsid
p22

### Envelope glycoproteins
E1 and E2 with highly variable region responsible for types and sub-types.

### Protease
Helicase to unwind the RNA

### Quasi-species
Rapid mutation rate; several genotypes: 1 to 6 with subtypes a, b,...; does not integrate into the genome of the host

### Hosts
Natural hosts: Only humans

### Source Human
Blood; internal fluids (CSF, pericardial, pleural, peritoneal, amniotic), semen, genital saliva and semen not identified; practically undetectable in stools and urine

### Environment
Rapidly degraded in the environment

### Transmission

- **Direct Parenteral exposure:** historically = serum hepatitis
  - Needle stick main mode of transmission to HCWs: risk 3% from hollow needle from infectious case
  - Parenteral drug users
  - Human bites: probably no risk
  - STD

- **Perinatal Transmission:** Infants seroconversion rate of 6%; related to [blood]; if mothers with >1,000,000 V/ml

- **In utero**

- **NOT transmitted:** aerosolized blood; Mucosal contact with saliva poses little if any risk

### Risks

| High risk groups | USA: 25% hepatitis cases = HCV; 1980s
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemophiliacs</td>
<td>50-90% 30,000 new infections (25-30% diagnosed); 500,000 total infections 1980s</td>
</tr>
<tr>
<td>Parenteral drug users</td>
<td>50-90% 10,000 new acute cases/year (1997)</td>
</tr>
<tr>
<td>Hemodialysis patients</td>
<td>20-90% incidence = 15 /100,000</td>
</tr>
<tr>
<td>High risk sexual behavior</td>
<td>1-10% 4-5 millions infected individuals</td>
</tr>
<tr>
<td>Sexual partner with HCV</td>
<td>1-10% illicit drug use</td>
</tr>
<tr>
<td>Household member with HCV</td>
<td>1-10% high-risk sexual behavior</td>
</tr>
<tr>
<td>Transfusion recipients: decline after 1985. 7% blood transfusion</td>
<td></td>
</tr>
<tr>
<td>HCW</td>
<td>1-5% 8-10,000 /year deaths</td>
</tr>
</tbody>
</table>

### Prevalence anti HCV %

- North America 0.5-1.5%
- Latin America, Caribbean 0.5-2%
- Western Europe 0.5-1%
- Middle East 0.5-3%
- Sub-Saharan Africa 5%
- Asia 0.5-3%
- Australia /Oceania 0.5%
- Highest: Egypt 15%, Tanzania 17%, Rwanda 17%, Cameroon 12%; Guinea 11%
- Mongolia 10%, Japan 2.3%

### Pathogenesis

#### HBV acute hepatitis

Clinical case: An acute illness with a) discrete onset of symptoms and b) jaundice or elevated serum aminotransferase levels

Laboratory criteria: Serum ALT >2.5 ULN + IgM-antiHBV positive + IgM-antiHAV neg + IgM-antiHBC neg or HBsAg negative

Confirmed: a case that meets the clinical case definition and is laboratory confirmed

Asymptomatic infection: mostly childhood infections

#### Acute Hepatitis B

Prodromal phase: malaise, weakness, anorexia, myalgia and arthralgia, macular rash (15-30%)

Few days: 30 jaundice; persists for weeks

#### Fulminant hepatitis

Hepatocyte lesions: Liver enzyme abnormalities

1% of adults with jaundice

### Serology

#### EIA 1

1990-92; used antibody to c100-3 epitope; appear within 1st year; sensitivity (TP/D) 50% at 6 weeks

#### EIA 2

After 1992; use 4 epitopes: c100-3, c22-3, c33c, 5-1-1; sensitivity (TP/D) 80% at 6 weeks, up to 92-95% later in disease

False positive in auto-immune disease; False negative: too early, hemodialysis or immunocompromised

Blood donor screening = EIA 2 for total IgG + IgM; window period (pre-positive) up to 22 weeks

### RIBA

Recombinant Immunoblot Assays: same antigen but in immuno-blot format; confirmatory test

### HCV-RNA qualitative

by reverse transcription polymerase chain reaction (RT-PCR); most sensitive; positive = confirmatory; negative does not prove non-infection; depends on viremic load

### HCV-RNA quantitative

No strong correlation between viremic load and intensity of chronic lesions

Commercially available assays have clinically relevant detection thresholds of approximately 100 viral genomes/mL of serum

### Serum conversion

Evident 2 weeks - 6 months following infection, with primates delayed seroconversion up to 5 years after exposure

### Serum ALT

Most simple and clearest way to assess disease activity; ALT levels fluctuate so 1 normal ALT does not exclude active hepatitis strong association between serum ALT levels and histopathological findings on the liver biopsies

### Time Line

#### Clinical

<table>
<thead>
<tr>
<th>EIA 1</th>
<th>EIA 2</th>
<th>HCV-RNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 weeks</td>
<td>8</td>
<td>12</td>
</tr>
</tbody>
</table>

### Liver biopsy

gold standard for assessment of chronic hepatitis; useful in judging the severity, stage of disease & degree of fibrosis.

### Viral isolation

cultures difficult, not routine;

### PH Lab

http://www.infectiousdisease.dhh.louisiana.gov

(800)256-2748
## Treatment
- interferon monotherapy
- interferon and ribavirin (a guanosine nucleoside analogue) combination therapy.
  - goal = sustained virologic clearance; Sustained response = no detectable HCV RNA 6 months after completion of tx
- Genotype 1b: only 10%-15% of interferon monotherapy effective; Genotypes 1a, 2a, 2b, 3a significantly higher long-term response

## Genotype & Tx

### PUBLIC HEALTH

<table>
<thead>
<tr>
<th>Case management</th>
<th>See below</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood, organ, semen donation</td>
<td>Blood &amp; blood products donor screening; required by law</td>
</tr>
<tr>
<td>Hemophiliacs</td>
<td>Heating factor VIII at 80°C for 72 hours</td>
</tr>
<tr>
<td>Tattoos, body piercing</td>
<td>Regulation</td>
</tr>
<tr>
<td>HCW BBFE</td>
<td>Screening; diagnosis; counseling; tx if indicated</td>
</tr>
<tr>
<td>I Control</td>
<td>Prevention of environmental transmission</td>
</tr>
<tr>
<td>Screening programs</td>
<td>Immigrants, refugees, children adopted from high risk areas</td>
</tr>
</tbody>
</table>

## Surveillance

<table>
<thead>
<tr>
<th>Report ACUTE CASES only</th>
<th>Fill CDC Form; verify lab tests (particularly IgM positive and not IgG or total anti-HAV;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure Hx</td>
<td>Contact w hepatitis pt; travel outside US; parenteral drug use; close contact w baby /young child home /work; employment in food svcs or health care; shellfish consumption</td>
</tr>
<tr>
<td>Vaccine &amp; serologic testing Hx</td>
<td>Prevention of environmental transmission</td>
</tr>
</tbody>
</table>

## Exclusion
None

## Isolation Precautions
- Universal precautions

## Case Management
- 1-Refer to PMD for case management; 2-Investigate source of disease; 3-Test & counsel contacts

## Medical Evaluation
- Rule out HAV, HBV & other hepatitis; Confirm HBV; Evaluate activity: sx, physical, ALT, ?biopsy?; tx if indicated

## Source Investigation
- Personal contact; Sexual partner; Blood product; Transplant; Dialysis; injectable Drug use; Occupational exp to BBF; Tattoos, body piercing

## Contact Investigation
- ID contacts (see source) Test contacts; HIGA /Vaccine for susceptible contacts
- Other cases in outbreak

## HCW / BBFE
- (National Hepatitis Detection and Treatment Program) test source for ALT
- If source unknown or anti-HCV+ or hi AST: exposed HCW baseline AST and anti-HCV.
- If initially negative, anti-HCV repeat at 3 & 6 months
- Counseling; Medical Tx if required; No ISG necessary since poor [anti-HCV]

## Counseling
- Prevent sexual transmission; Do not donate blood; Avoid parenteral ctc: needles, tattoos, body piercing

## Information
- Hepatitis Hotline of the Hepatitis Branch, CDC at 1-888-4HEP-CDC (or 1-888-443-7232)
- National Immunization Program, CDC Information Hotline at 1-800-232-2522
- CDC Hepatitis Branch website at http://www.cdc.gov/ncidod/diseases/hepatitis/
- CDC National Immunization Program website at http://www.cdc.gov/nip

---

http://www.infectiousdisease.dhh.louisiana.gov

(800)256-2748