HEPATITIS C

Virology	Flavivirus RNA single strand envelope **1988**
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 → 36% **In utero** **NOT transmitted:** aerosolized blood; Mucosal contact with saliva poses little if any risk **Households** of chronically infected: low transmission w **Environmental transmission:** minimal **Inapparent transmission**: 40% unexplained by any risk factor

Risks				**Prevalence anti HCV %**	
High risk groups		**USA:** 25% hepatitis cases = HCV;		North America	0.5-1.5%
Hemophiliacs	50-90%	30,000 new infections (25-30% diagnosed);		Latin America, Caribbean	0.5-2%
Parenteral drug users	50-90%	10,000 new acute cases/year (1997)		Western Europe	0.5-1%
Hemodialysis patients	20-90%	incidence = 15 /100,000		Middle East	0.5-3%
High risk sexual behavior	1-10%	4-5 millions infected individuals		SubSaharan Africa	5%
Sexual partner with HCV	1-10%	illicit drug use	60%	Asia	0.5-3%
Household member with HCV	1-10%	high-risk sexual behavior	15%	Australia /Oceania	0.5%
Transfusion recipients: decline after 1985.	7%	blood transfusion	7%	Highest: Egypt 15%, Tanzania 17%, Rwanda 17%, Cameroon 12%; Guinea 11% Mongolia 10%, Japan 2.3%	
HCW	1-5%	8-10,000 /year deaths			
M:F ratio is 1:1					

Pathogenesis	
Incubation	15 days – 180 days (2 weeks - 6 months, mean 8 weeks)
Communicability	HCV RNA in blood 1 to 3 weeks before onset; may persist indefinitely in 85%; viremia correlates loosely w ALT activity at first
Definition	
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-antiHCV positive + IgM-antiHAV neg + IgM-antiHBc neg or HBsAg negative Confirmed: a case that meets the clinical case definition and is laboratory confirmed
Clinical	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 Hepatocyte lesions: Liver enzyme abnormalities
Fulminant hepatitis	1% of adults with jaundice
Chronic infection	
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
Seroconversion	evident **2 weeks - 6 months following infection**, with primates delayed seroconversion up to 5 years after exposure
Serum ALT	most simple and cheapest way to assess disease activity; ALT levels fluctuate so 1 normal ALT does not exclude active hepatitis weak association between serum ALT levels and histopathological findings on the liver biopsies

Time Line										
	Clinical									
	EIA 1		50%	±	60%	+	+	+	+	+
	EIA 2		80%	++	++	90%	+++	++	++	+
	HCV-RNA	days	+	++	++	++	++	++	++	+
		4 weeks	8	12	16	24	1 Year	2	3	10

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	

Treatment	interferon monotherapy
Genotype & Tx	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 monotx effective; Genotypes 1a, 2a, 2b, 3a significantly higher long-term response
PUBLIC HEALTH	
Case management	See below
Blood, organ, semen donation	Blood & blood products donor screening; required by law
Hemophiliacs	Heating factor VIII at 80°C for 72 hours
Tattoos, body piercing	Regulation
HCW BBFE	Screening; diagnosis; counseling; tx if indicated
IControl	Prevention of environmental transmission
Screening programs	Immigrants, refugees, children adopted from high risk areas
Surveillance	
	Report ACUTE CASES only; Fill CDC Form; verify lab tests (particularly IgM positive and not IgG or total anti-HAV; **Exposure Hx:** 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 **Vaccine & serologic testing Hx**
Exclusion	None
Isolation Precaution	**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, bodypiercing
Contact Investigation	ID contacts (see source) Test contacts; HBIG /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