



Hepatitis C The Long Term Care Risk

THE ELEVENTH ANNUAL INTERCOMPANY LONG TERM CARE INSURANCE CONFERENCE

ILTCl



Objectives

- Basics of the disease
- Disease progression
- Comorbid factors
- Treatment
- Long term care risk



Basics of Hepatitis C

- Caused by an RNA virus
- Clinical Course
 - Acute
 - 5 weeks from infection
 - Increased SGOT, SGPT
 - Chronic
 - Defined as infection for more than 6 months
 - Acute becomes chronic ~ 85% of the time



Hepatitis C – Case #1

- 62 yo M applying alone for comprehensive coverage \$200/d, 5yr BP, 90 d EP
- Mild ^ ALT/AST for many years
- Hepatitis C diagnosed by Hepatitis C Ab +
- Had transfusion in his 30's after an accident



Hepatitis C – Case #1 cont'd

- Age 56 (2004) – liver biopsy:
 - Mild inflammation, no fibrosis
- Age 60 (2008) repeat liver biopsy:
 - Grade 1 inflammation (activity)
 - Stage 2 fibrosis – portal fibrosis with some septal fibrosis
- Genotype 1b
- Treatment begun with pegylated interferon and ribavirin
- 4 weeks – viral RNA load undetectable, AST/ALT normalized



Hepatitis C – Case #1 cont'd

- Treated for 48 weeks
- Hepatitis C RNA by PCR negative at 6 months after treatment completed
- AST/ALT continue to be normal
- Serum albumin above 4.0



Hepatitis C – Transmission

Had transfusion in his 30's after an accident

- Transfusion prior to blood pool testing for Hep C ~1990
- IV drug use
- Cocaine (intranasal)
- Multiple sexual partners
- Tattoos
- Acupuncture
- Razor sharing
- Needle stick injury (health care providers)
- Unknown (~10%)



Liver Biopsies

- Age 56 (2004) – liver biopsy:
 - Mild inflammation, no fibrosis
 - Grade 1, Stage 0
- Age 60 (2008) repeat liver biopsy:
 - Grade 1 inflammation (activity)
 - Stage 2 fibrosis – portal fibrosis with some septal fibrosis



Hepatitis C – Liver Biopsy Staging

- Grade - degree of inflammation
 - Grades 1-4 (*a little to a lot*)
- Stage – degree of fibrosis
 - 0: No fibrosis
 - 1: Portal fibrosis
 - 2: Periportal fibrosis/rare septal fibrosis
 - 3: Septal fibrosis/bridging fibrosis
 - 4: Cirrhosis



Grade of Liver Inflammation

Grade	Description	Degree of Interface Hepatitis (Piecemeal necrosis)	Degree of Lobular Inflammation
0	Portal inflammation only, no necrosis	None	None
1	Minimal necrosis	Minimal, patchy	Minimal, patchy
2	Mild necrosis	Mild involving some or all portal tracts	Mild hepatocellular damage
3	Moderate necrosis	Moderate involvement of all portal tracts	Moderate, noticeable hepatocellular damage
4	Severe necrosis	Severe with bridging necrosis	Severe, diffuse hepatocellular damage

Stage of Liver Fibrosis

Stage	Description	Criteria
0	No fibrosis	Normal connective tissue
1	Portal fibrosis	Fibrous portal expansion
	Perisinusoidal fibrosis	Consider as early Stage 1 if an isolated finding
2	Periportal fibrosis	Periportal or rare portal to portal septa
3	Septal fibrosis Bridging fibrosis	Portal to portal septa, bridging architectural distortion, no cirrhosis
4	Cirrhosis	Extensive fibrosis with regenerative nodules



Liver Schematic

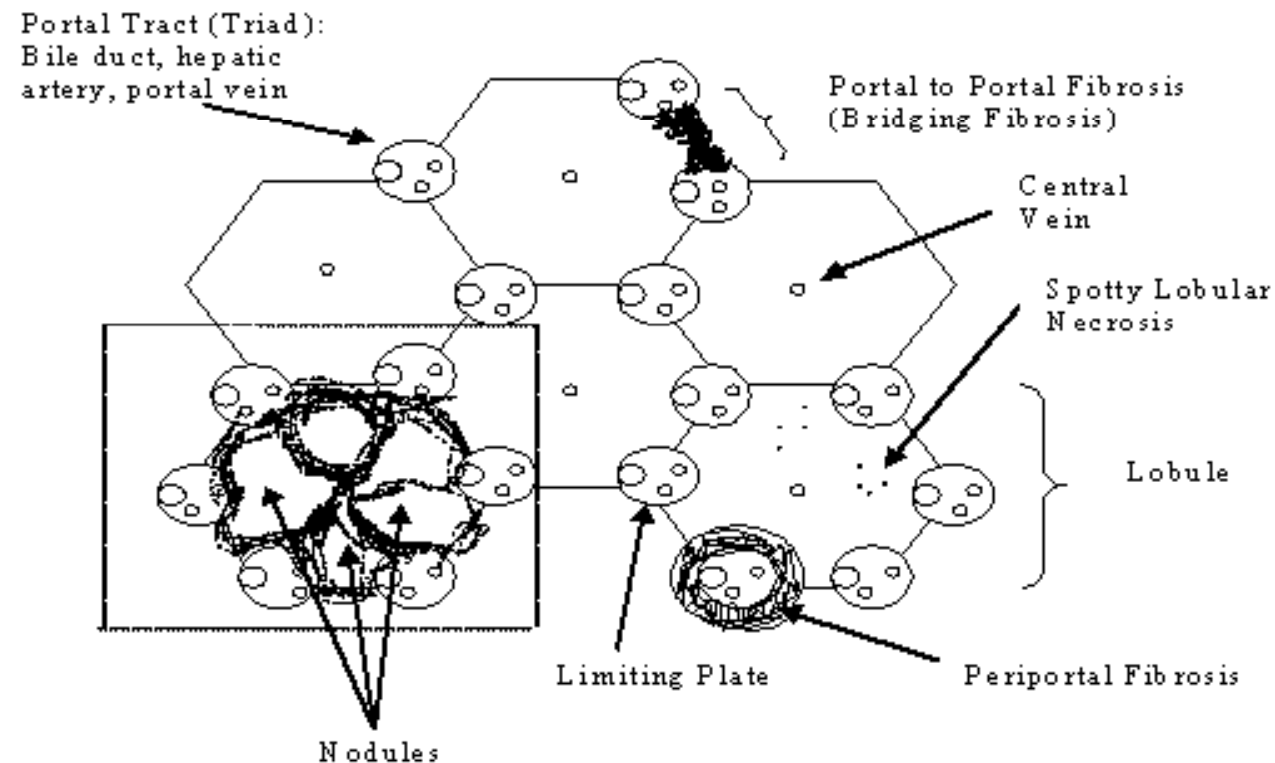
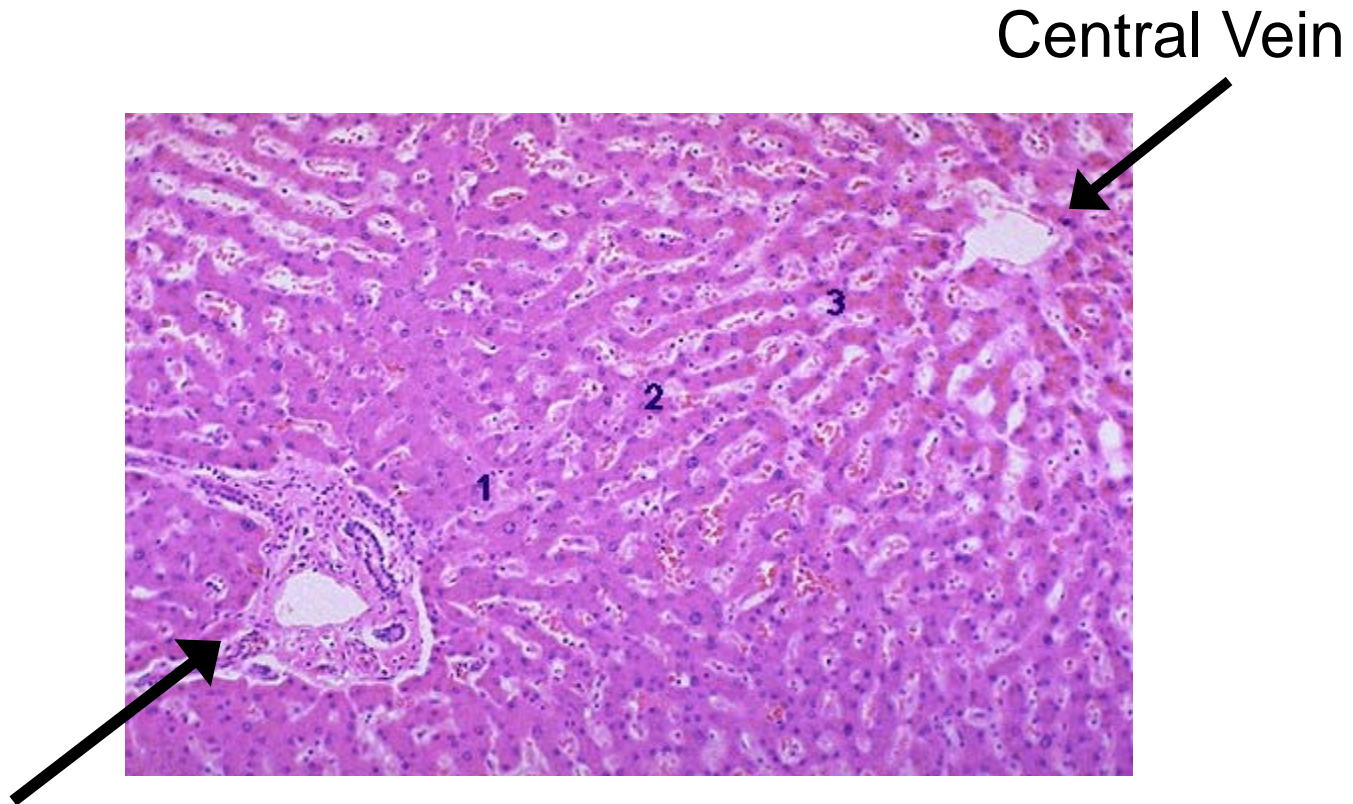


Figure 1. Schematic representation of liver histology with various pathologic changes. Area within the dotted lines demonstrates cirrhosis. Portal to portal and portal to central fibrosis results in nodule formation.



Normal Liver

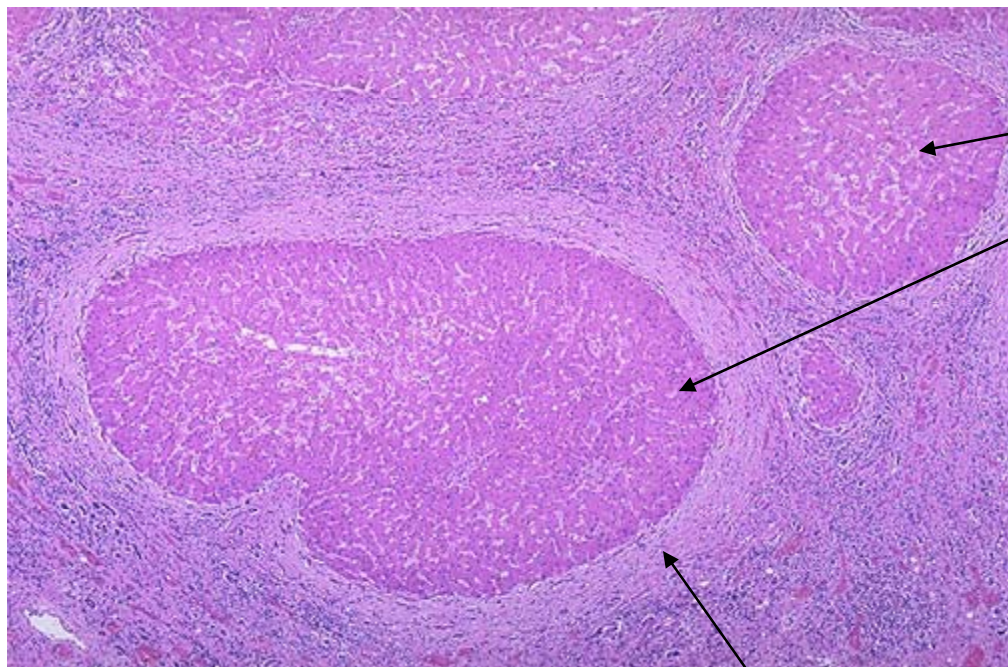


Central Vein

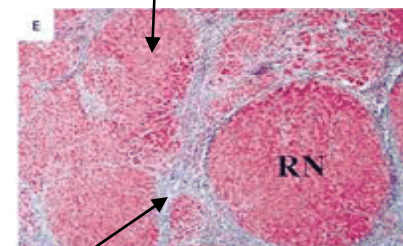
Portal Triad:
Bile duct, hepatic
artery, portal vein



Cirrhosis



Liver cells



Bands of scar tissue surround groups of liver cells

*RN =
regenerative
nodule*



Hepatitis C – Progression

Had transfusion in his 30's

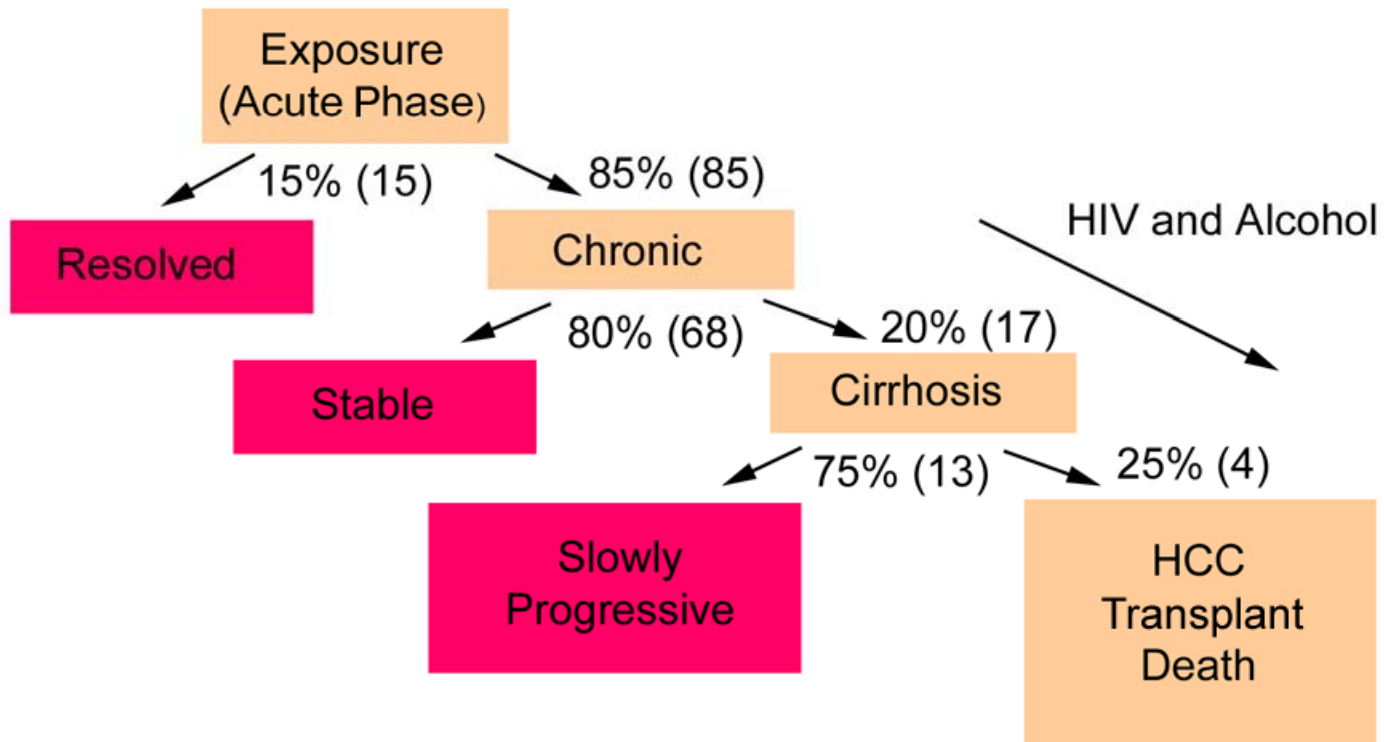
Disease for 30+ years ?

- Biopsy #1 Grade 1/Stage 0
 - Mild disease especially after 30 years
 - ? Risk of progression
 - Do transaminases help predict degree of liver disease/progression?
 - **NO**
- Biopsy #2 Grade 1/Stage 2
 - More progression than would be expected
 - Why?



Progression

Natural History of HCV Infection



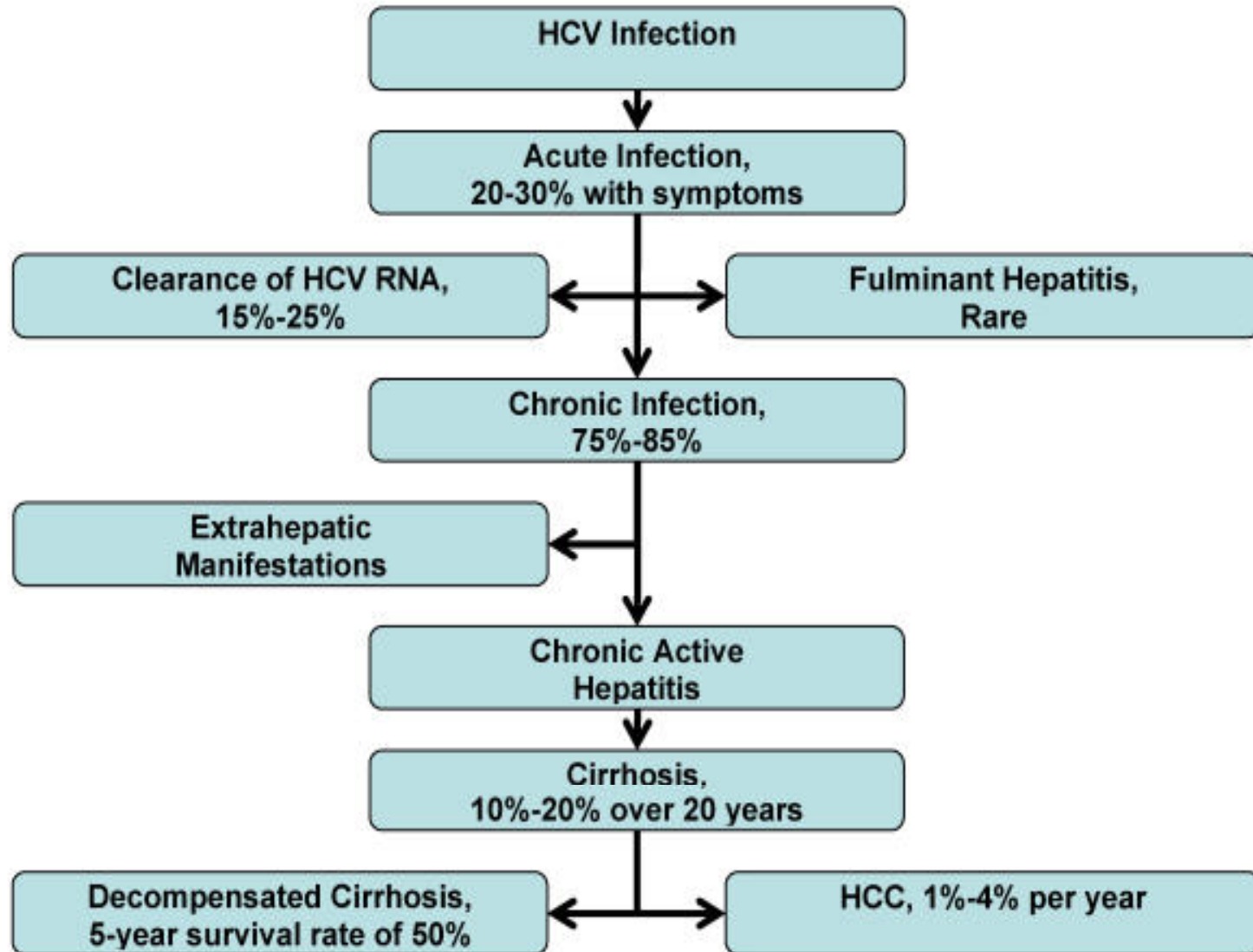


Progression Predictors

- Alcohol use (>3 drinks/d in males, >2/d in females)
- Excess iron stores
- Male
- Immunosuppression (HIV)
- Concomitant hepatitis (e.g., Hepatitis B)
- Age of acquisition (> age 40)
- Other liver disease



Progression Prediction

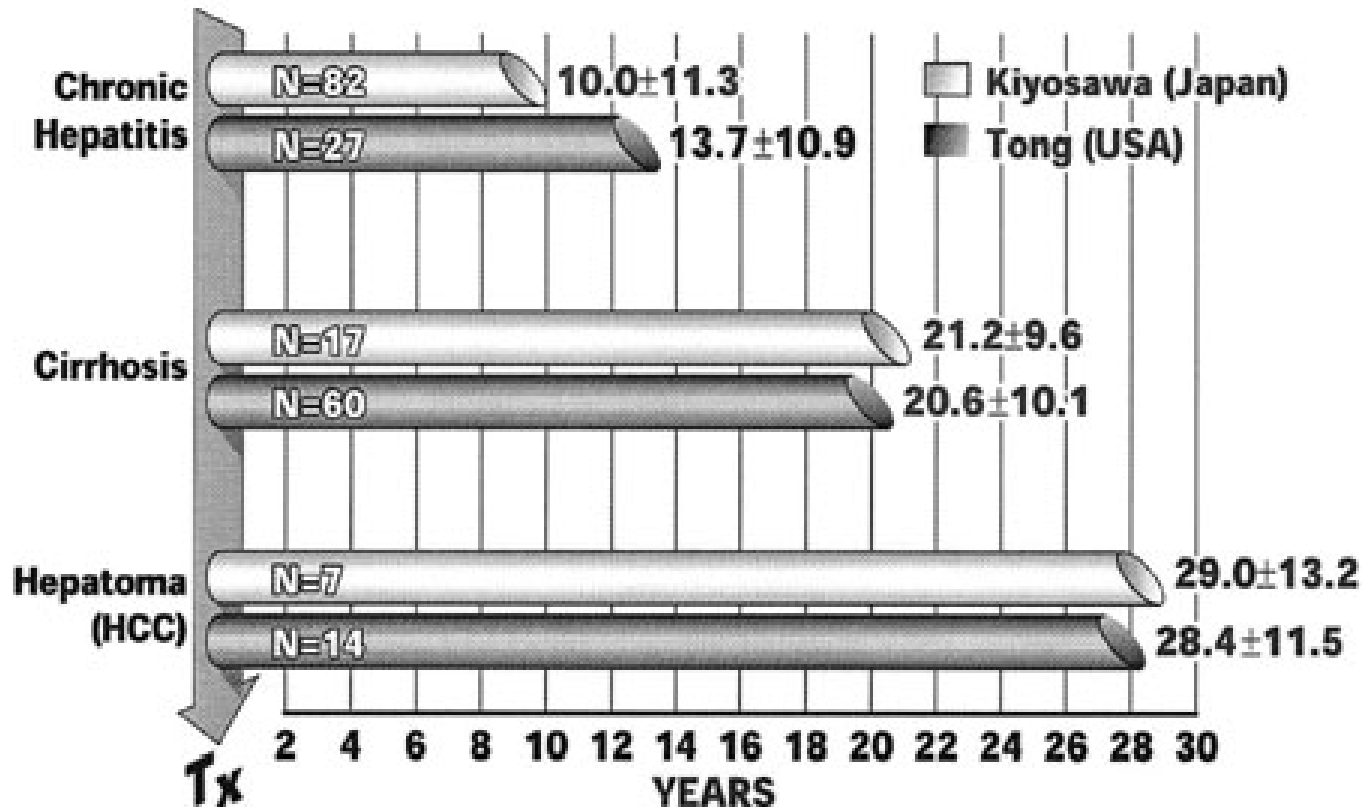


[*Int J Med Sci.* 2006; 3\(2\): 47–52.](#)



Progression Prediction

Medscape® www.medscape.com



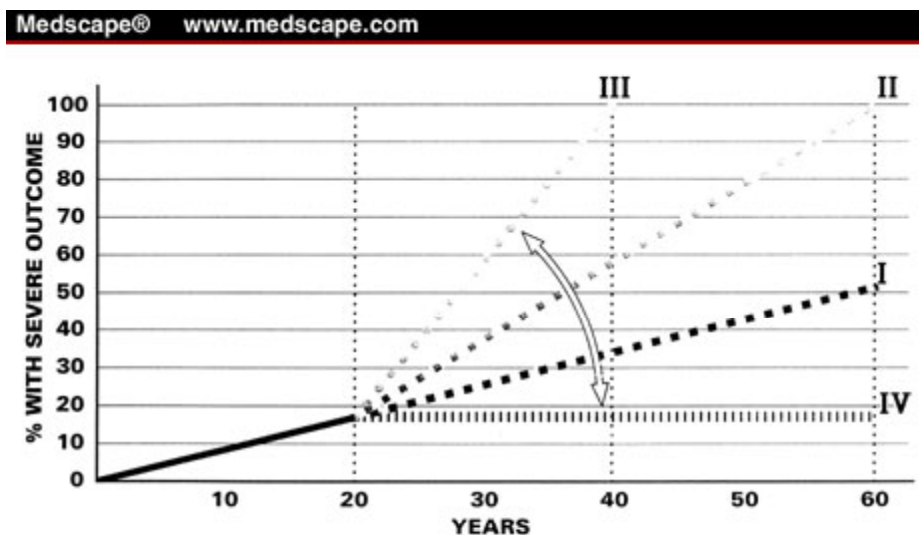
The time course of HCV-related disease in two retrospective studies that performed liver biopsies on referred patients with a past history of blood transfusion. The indicated duration of disease was based on the interval from the time of transfusion to the time of liver biopsy.

Semin Liver Dis. 2000;20(1) Recovery, Persistence, and Sequelae in Hepatitis C Infection: A Perspective on Long-term Outcome. Harvey J. Alter, MD and Leonard B. Seef, MD



Progression Prediction

- Dilemma
 - Is progression linear?
 - Is it level and then gets worse?
 - Is it level and stays on the same trajectory?
 - Is it level and then resolves?



Semin Liver Dis. 2000;20(1) Recovery, Persistence, and Sequelae in Hepatitis C Infection: A Perspective on Long-term Outcome. Harvey J. Alter, MD and Leonard B. Seef, MD



Hepatitis C Treatment

- Medications
 - Pegylated interferon (injectable)
 - Ribavirin (tablets)
- Treatment Regimens
 - 24 weeks – genotypes 2, 3
 - 48 weeks – genotype 1b (most common in US)
 - higher stages of fibrosis
- Follow up with viral load looking for decreasing viral count



Treatment Response Predictors

- Genotype
 - Type 1a and b (most common in US) and type 4 (not very common)
 - Most resistant to current treatment (~45%)
 - Type 2 and 3 significant minority
 - More responsive to treatment (~85%)
- Initial viral load
- Degree of fibrosis
- Obesity
- Gender



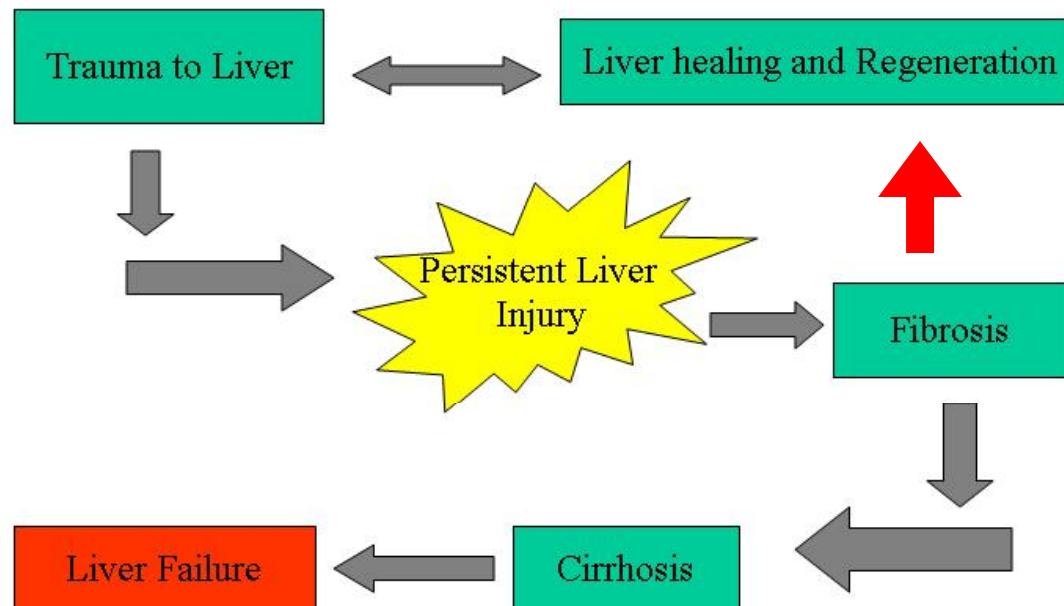
Treatment Goals

- Sustained viral response (SVR)
 - No detectable viral RNA 6 months after treatment completed
- Improvement in liver histology
 - Arrest or improve fibrosis



The Path of Liver Disease

MCU1

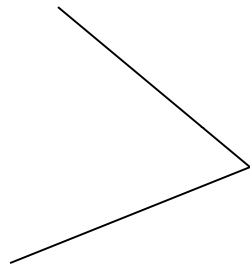


Progression of Liver Disease



Long Term Care Risk of Treatment

- Treatment
 - Short term
 - Fatigue
 - Depression
 - Anemia
 - Long term
 - None known



? Effect on ADL's



Long Term Care Risk of Disease

- Short term
 - Fatigue
- Long term
 - Risk of relapse
 - Rare if at all
 - Risk of cirrhosis in this individual
 - Does fibrosis improve?
 - LTC risk if disease arrested
 - LTC risk of cirrhosis
 - Encephalopathy
 - Upper GI bleeding
 - Ascites
 - Hepatocellular carcinoma
 - Transplantation
 - Sleep disturbance
 - Pruritis



Long Term Care Risk of Disease

Extrahepatic manifestations

- Cryoglobulinemia
- Weakness, arthralgias, and purpura; (often related to vasculitis)
- Membranoproliferative glomerulonephritis
- Idiopathic thrombocytopenic purpura
- Lichen planus
- Keratoconjunctivitis sicca
- Raynaud syndrome
- Sjogren syndrome
- Porphyria cutanea tarda
- Necrotizing cutaneous vasculitis
- Non-Hodgkin lymphoma



Hepatitis C – Case #2

- 62 yo F \$150/d comprehensive 90 d EP
- Hx of long standing *mild* ^ *ALT/AST* (50-70/50-70, *occasionally normal*)
- Hx of Hepatitis C *dx'ed 10-15 years ago* with *liver biopsy 10-15 years ago – minimal inflammation, no fibrosis*
- *No treatment* based on mild biopsy findings
- Current labs: AST/ALT 62/71, *alb. 4.4*, CBC nl, *MCV 95, plts 235*

What are the LTC concerns?

Disease progression? Treatment risk?



Hepatitis C – Case #2 cont'd

- Build: BMI 33
 - Steatohepatitis
 - ? Treatment resistance
- Drinks 2-3 glasses wine/night
- Sibling with hemochromatosis
 - One in four chance of having it too



Hepatitis C – Summary - Pearls

- Long course – “often die with rather than as a result of”
- Traditional LFT’s (ALT/AST) not useful for disease severity prediction
- Hepatitis C antibody is forever
- Viral load does not predict disease course
- Treatment can be curative
- Fibrosis is reversible (if not cirrhotic)



Hepatitis B

The Long Term Care Risk

March 7, 2011



Session Goals

- Understand the progression of liver disease with chronic hepatitis B
 - hepatitis B infection
 - epidemiology
 - classification of infection
 - current treatment
 - prognosis
 - favorable/unfavorable factors
- Describe the impact of co-morbid factors on the progression of chronic hepatitis B
 - hepatitis C/D/HIV
- Describe the long term care risk of chronic hepatitis B
 - cirrhosis
- Describe the impact of chronic hepatitis B on long term care claims
 - LTCi experience
- Case studies
- Summary



Case #1

- 56 yo Female of Asian Descent for Well Exam. Recalls Abnormal Hepatitis Test in Past.
- Current Labs:
 - AST 33; ALT 40; Serum Albumin wnl; AFP wnl
 - HBsAg +; HBeAg -; anti-HBeAg +
 - HBV DNA 1,000 IU/ml
 - No Liver Biopsy
- Prior Labs:
 - LFTs 5 Years Ago WNL
- Questions:
 - Risk For Progressive Liver Disease (Low – Medium – High)?
 - What Should Be Done Next?



Case #2

- 62 yo Male – History of Treated Chronic HBV
 - Diagnosed After Abnormal LFTs on Life Insurance Exam
 - History of Multiple Tattoos
- Findings Prior to Treatment
 - AST 97; ALT 125; Serum Albumin wnl; AFP wnl
 - HBsAg +; HBeAg +; anti-HBe Ag –
 - HBV DNA 200,000 IU/ml
 - Liver Biopsy – Grade 2 Inflammation; Stage 1 Fibrosis
- Treated
 - Pegylated Interferon X 48 wks; HBeAg – at 24 and 48 wks
- Current Labs 18 Months Later
 - AST 35; ALT 38; HBsAg +; HBeAg -; anti-HBeAg +
 - HBV DNA Undetectable
 - Liver Biopsy – Grade 1 Inflammation; Stage 1 Fibrosis
- Questions
 - Risk For Progressive Liver Disease (Low – Medium – High)?



Hepatitis B Virus (HBV)

- DNA virus - small, circular
- 8 genotypes (A-H); A-C account for 88% cases in US
- transmission: perinatal, percutaneous (injection), sexual exposure and close person-to-person contact (open cuts/sores), unscreened transfusions
- virus can survive at least 7 days outside the body
- incubation 60-150 days
- symptoms: anorexia, nausea, vomiting, abdominal pain and jaundice
- rash, joint pain, arthritis may occur
- case fatality rate of acute hepatitis B is 1%
- 95% adults will fully recover
- 30-90% young children; <5% adults will develop chronic HBV infection
- vaccination highly effective

<http://www.cdc.gov>



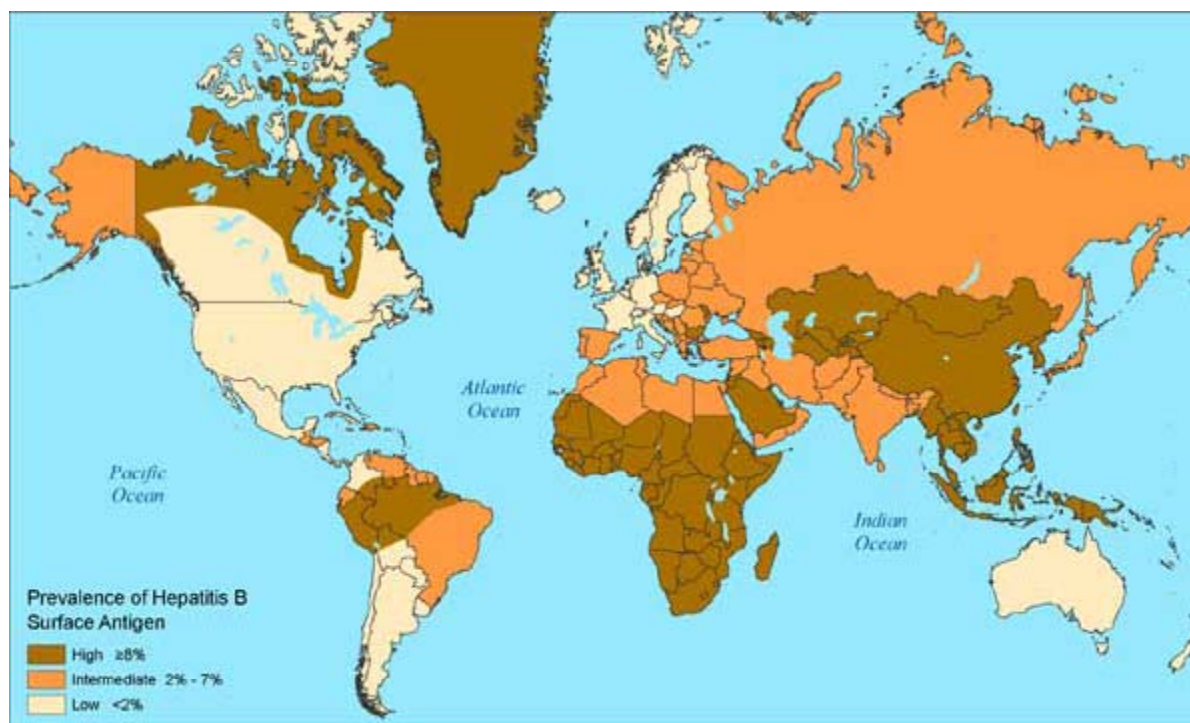
Epidemiology

- 350 million worldwide chronically infected
- 43,000 new infections reported 2007; 4,519 cases of acute disease
- 1.25 million in US carriers of HBV
 - US prevalence chronic HBV <2%
- 15-40% will develop serious sequelae during their lifetime (chronic liver disease including cirrhosis, liver failure or liver cancer)
- estimated 3,000 persons in US die/year from HBV-related illness
- rate of new HBV infections has declined 82% since 1991 when routine vaccination of children was first recommended

<http://www.cdc.gov>; Lok AS, McMahon BJ. *Hepatology* 2007;45:507



Epidemiology



<http://www.cdc.gov>



Classification of Infection

- Definitions

- Chronic HBV
 - chronic necroinflammatory liver disease (HBeAg + and HBeAg -)
- Inactive HBsAg Carrier State
 - persistent infection without liver disease
- Resolved HBV
 - no evidence active virus infection (HBsAg -)
- Acute Flare of HBV
 - intermittent LFT elevation >10 X normal
- Reactivation of HBV
 - reappearance of inflammatory liver disease in person felt to be carrier or have resolved infection
- HBeAg Clearance
 - loss of HBeAg
- HBeAg Seroconversion
 - loss of HBeAg and detection of anti-HBe
- HBeAg Reversion
 - reappearance HBeAg in person previously HBeAg – and anti-HBe +

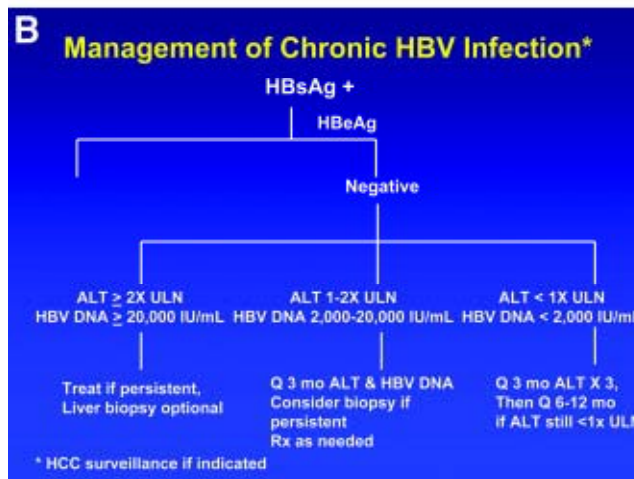
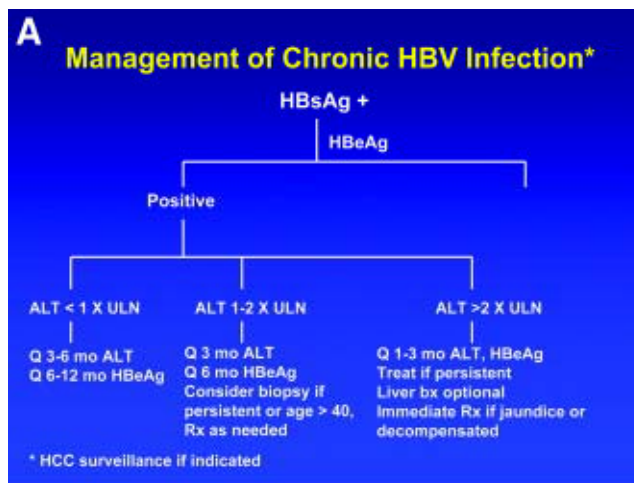
- Diagnostic Criteria

- Chronic HBV
 - HBsAg + > 6 months
 - HBV DNA >20K IU/ml (2K-20K often seen HBeAg – HBV)
 - persistent/intermittent elevation AST/ALT levels
 - moderate-severe necroinflammation on liver biopsy
- Inactive HBsAg Carrier State
 - HBsAg + > 6 months
 - HBeAg - , ant-HBeAg +
 - HBV DNA <2K IU/ml
 - persistently normal AST/ALT
 - absence of hepatitis in liver biopsy
- Resolved HBV
 - previous infection or presence of anti-HBc +/- anti-HBs
 - HBsAg –
 - undetectable HBV DNA
 - normal ALT

Lok AS, McMahon BJ. *Hepatology* 2007;45:507



Management



Lok AS, McMahon BJ. *Hepatology* 2007;45:507



Current Treatment

Table 1. Currently Used or Approved Antiviral Therapies for HBeAg-Positive Chronic HBV Infection in Patients Who Have Not Received Treatment.*

Variable	Pegylated Interferon Alfa-2a (Pegasys) [†]	Lamivudine (Epivir)	Adefovir (Hepsera)	Entecavir (Baraclude)	Telbivudine (Tyzeka)	Tenofovir (Viread)
Route of administration	Subcutaneous	Oral	Oral	Oral	Oral	Oral
Dose	180 µg/wk	100 mg/day [‡]	10 mg/day [‡]	0.5 mg/day [‡]	600 mg/day [‡]	300 mg/day [‡]
Duration of therapy — wk [§]	48	48 to ≥52	≥48	≥48	≥52	≥48
Tolerability	Influenza-like symptoms (e.g., fatigue, fever, and myalgias), cytopenias, depression, anxiety, irritability, autoimmune disorders	Well tolerated	Well tolerated, but creatinine monitoring advisable	Well tolerated	Well tolerated	Well tolerated, but creatinine monitoring advisable
HBeAg seroconversion — % [¶]						
At 1 yr	27 (32 at 72 wk)	16–21	12	21	22	21
At >1 yr	NA	Up to 50 at 5 yr	43 at 3 yr	39 at 3 yr	30 at 2 yr	ND
Serum HBV DNA — mean or median reduction in log ₁₀ copies/ml at 1 yr	4.5	5.5	3.5	6.9	6.4	6.2
Serum HBV DNA undetectable by PCR — %	25	36–44	13–21	67	60	80
ALT normalization at end of 1 yr — %	39	41–75	48–61	68	60	77
HBSAg loss — %						
At 1 yr	3	≤1	0	2	<1	3
At 2 yr	NA	3	ND	5	ND	5 at wk 64
Histologic improvement — % ^{**}	38 at wk 72	49–62	53–68	72	65	74
Viral resistance — %						
At 1 yr	None	15–30	None	None ^{††}	6	0
At >1 yr	NA	70 at 5 yr	ND	<1% up to 4 yr	22	ND
Durability of the HBeAg response after 1 yr — % ^{‡‡}	82	70–80	91	82	80	ND
Approximate cost for 1 yr of treatment — \$ ^{§§}	18,000	2,500	6,500	8,700	6,000	6,000
Strength or weakness	Finite duration, no resistance, 1-yr serologic advantage, injectable, low tolerability	Oral, well tolerated, moderate potency, high resistance	Oral, well tolerated, modest potency, moderate resistance	Oral, well tolerated, high potency, low resistance	Oral, well tolerated, high potency, high resistance	Oral, well tolerated, high potency, low resistance

* Data were derived from assessment of these drugs versus placebo or versus an active study drug in registration clinical trials; in most cases, these comparisons were not based on head-to-head testing of the different drugs. In addition, the sensitivity and dynamic range of virologic assays differed across trials, as did definitions of and criteria for drug resistance. ALT denotes alanine aminotransferase, HBeAg hepatitis B e antigen, HBSAg hepatitis B surface antigen, NA not applicable, ND no data available, and PCR polymerase chain reaction.

† Standard interferon alfa is also an approved therapy for chronic HBV infection, but unlike pegylated interferon, which is administered once a week, standard interferon is administered daily or three times a week and is less effective. In addition, most clinical trials of standard interferon relied on insensitive assays for HBV DNA levels, which are not comparable to HBV DNA levels reported for the other drugs on the basis of contemporary HBV DNA assays. Since pegylated interferon has replaced standard interferon, standard interferon is not included in this comparison of antiviral agents. Pegylated interferon alfa-2a is the only pegylated interferon approved in the United States for use in patients with HBV infection; however, pegylated interferon alfa-2b is approved for the treatment of HBV infection in several other countries. Recommendations for weight-based dosing of pegylated interferon alfa-2b are found in the product brochure.

‡ The dose should be adjusted downward for patients with reduced creatinine clearance, per the manufacturer's recommendation.

§ The duration shown is the duration of therapy in clinical efficacy trials.

¶ The frequency of HBeAg seroconversion (loss of HBeAg and acquisition of anti-HBe) is reported at the end of 1 year of therapy in registration trials and at the end of additional years of therapy, when data are available. For pegylated interferon, 32% HBeAg seroconversion was recorded at week 72 (24 weeks after the discontinuation of therapy). For adefovir, HBeAg seroconversion after year 1 was based on a Kaplan-Meier estimate in a subgroup of study subjects.

|| Serum HBV DNA was considered to be undetectable by PCR if there were less than 300 to 400 copies per milliliter (<1000 copies per milliliter for adefovir) at the end of year 1.

** Histologic improvement is defined as a reduction of 2 or more points in the histologic activity index at year 1.

†† In lamivudine-resistant patients, viral resistance was 7% during year 1 of therapy and up to 43% at year 4. If entecavir is to be used in such patients, the approved dose is 1 mg per day.

‡‡ For HBeAg responses to oral agents, durability is shown after a period of additional consolidation therapy. The duration of consolidation therapy and the time when durability was assessed differed widely among studies; therefore, caution is warranted in interpreting these data. In patients treated for 48 weeks with pegylated interferon alfa-2a, 72 of 271 subjects (27%) had HBeAg seroconversion at week 48; in 13 of these 72 subjects (18%) followed for 24 weeks after therapy, HBeAg seroconversion responses were lost, so the durability frequency was 82%.

§§ The costs of therapy were derived from Hoofnagle et al.⁶

Dienstag J. N Engl J Med 2008;359:1486-1500



Current Treatment

Table 2. Currently Used or Approved Antiviral Therapies for HBeAg-Negative Chronic HBV Infection in Patients Who Have Not Received Treatment.*

Variable	Pegylated Interferon Alfa-2a (Pegasys) [†]	Lamivudine (Epivir)	Adefovir (Hepsera)	Entecavir (Baraclude)	Telbivudine (Tyzeka)	Tenofovir (Viread)
Serum HBV DNA — mean or median reduction in log ₁₀ copies/ml at 1 yr	4.1	4.2–4.7	3.9	5.0	5.2	4.6
Serum HBV DNA undetectable by PCR — % [‡]	63	60–73	51–64	90	88	95
ALT normalization at end of 1 yr — %	38	62–79	48–77	78	74	79
HBsAg loss — %						
At 1 yr	4	≤1	0	<1	<1	0
At >1 yr	8 at 3 yr after completion of 1 yr of therapy	ND	5 at 4–5 yr	ND	ND	ND
Histologic improvement — % [§]	48 at wk 72	61–66	64	70	67	72
Viral resistance — %						
At 1 yr	None	15–30	None	None	4	0
At >1 yr	NA	70 at 5 yr	29 at 5 yr	<1 up to 4 yr	9	ND
Durability of the HBV DNA–ALT response after 1 yr — % [¶]	18	<10	<10	ND	ND	ND

* Data were derived from assessment of these drugs versus placebo or versus an active study drug in registration clinical trials; in most cases, these comparisons were not based on head-to-head testing of the different drugs. ALT denotes alanine aminotransferase, HBeAg hepatitis B e antigen, HBsAg hepatitis B surface antigen, NA not applicable, ND no data available, and PCR polymerase chain reaction.

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[§] Histologic improvement is defined as a reduction of 2 or more points in the histologic activity index at year 1.

[¶] The durability of the HBV DNA–ALT response is shown after a period of additional consolidation therapy. The duration of consolidation therapy and the time when durability was assessed differ widely among studies; therefore, caution is warranted in interpreting these data.

Dienstag J. N Engl J Med 2008;359:1486-1500



Prognosis

- 95 % adults with acute HBV resolve without complication
- majority of carriers eventually lose HBeAg and develop anti-HBeAg
- perinatal acquired HBV who are HBeAg+/high HBV DNA levels/normal ALT – “immune tolerant” phase – many will develop chronic hepatitis with elevated ALT later in life
- carriers with elevated ALT will clear HBeAg at rate 8-12%/year
- after HBeAg conversion, 67-80% have low/undetectable HBV DNA, normal LFT, no inflammation on biopsy – “inactive carrier”
- 10-20% inactive carriers will reactivate with episodes of hepatitis years after quiescence
 - HBeAg- chronic hepatitis with HBV DNA >2K IU/ml, elevated LFT – tend to be older with more advanced liver disease. probable HBV variant
- clearance of HBeAg reduces the risk of hepatic decompensation and improves survival
- hepatocellular may occur after clearance of HBsAg – usually older with significant liver disease

<http://www.cdc.gov>; Lok AS, McMahon BJ. *Hepatology* 2007;45:507



Favorable Factors

- Favorable
 - HBsAg -
 - HBeAg -; anti-HBeAg +
 - normal LFT
 - undetectable HBV DNA
 - normal to minimal changes on biopsy – no evidence active inflammation

<http://www.cdc.gov>; Lok AS, McMahon BJ. *Hepatology* 2007;45:507



Unfavorable Factors

- Unfavorable
 - cirrhosis
 - older age
 - HBV genotype C
 - high DNA levels
 - alcohol
 - concurrent HCV/HDV
 - immunodeficiency

<http://www.cdc.gov>; Lok AS, McMahon BJ. *Hepatology* 2007;45:507



Unfavorable Factors

- Unfavorable
 - hepatocellular carcinoma (HCC)
 - males, older age
 - alcohol
 - family history HCC
 - reversion from anti-HBeAg to HBeAg
 - cirrhosis
 - HBV genotype C
 - concurrent HCV
 - adults with chronic HBV acquired in perinatal period (5%/decade – 100 X uninfected population)

<http://www.cdc.gov>; Lok AS, McMahon BJ. *Hepatology* 2007;45:507



Co-Morbid Issues

- Hepatitis C
 - 10-15% those with chronic HBV
 - increased rate of cirrhosis and HCC
- Hepatitis D
 - dependent on HBV for replication
 - most common Mediterranean and South America
 - more severe acute infection with higher mortality
 - chronic co-infection increases rate of cirrhosis, hepatic decompensation and HCC
- HIV
 - 6-13% those with HIV
 - more severe liver disease and increased rates liver related mortality

Lok AS, McMahon BJ. *Hepatology* 2007;45:507



Long Term Risk - Cirrhosis

Incidence of cirrhosis by HBV-DNA level

HBV-DNA level, copies/ml	Sample size	Person-yr follow-up	Cirrhosis cases	Incidence (per 100,000 person-yr)	Adjusted relative risk (95% CI) ^a
Undetectable ^b	869	10,048.8	34	338.8	Reference
300-9.9X10 ³	1150	13,259.0	57	429.9	1.4 (0.9-2.2)
1.0-9.9X10 ⁴	628	7105.5	55	774.0	2.5 (1.6-3.8) ^c
1.0-9.9X10 ⁵	333	3460.0	65	1878.6	5.9 (3.9-9.0) ^c
=1.0X10 ⁶	602	6164.3	154	2498.3	9.8 (6.7-14.4) ^c

^a Adjusted for age, sex, cigarette smoking, and alcohol consumption

^b <300 copies/ml

^c P <.001; test of trend P < .001

Iloeje UH, et al. *Gastroenterology* 2006;130:678



Long Term Risk - Cirrhosis

Association between HBV DNA level and cirrhosis risk stratified by several variables

Adjusted relative risk ^a (95% confidence interval) for HBV DNA in copies/ml					
Variables	<300	300-9.9X10 ³	1.0-9.9X10 ⁴	1.0-9.9X10 ⁵	≥10 ⁶
Sex					
Female	Reference	1.2 (0.5-2.9)	0.9 (0.3-2.7)	7.4 (3.0-18.3)	10.3 (4.8-22.0)
Male	2.2 (1.0-4.9)	3.3 (1.6-7.1)	6.7 (3.1-14.2)	12.7 (6.0-26.9)	21.3 (10.3-44.1)
Age					
≤50	Reference	1.0 (0.5-1.7)	1.6 (0.9-2.8)	3.4 (2.0-5.9)	5.0 (3.1-8.0)
>50	0.8 (0.4-1.6)	1.7 (1.0-3.0)	3.3 (1.9-5.8)	8.2 (4.8-14.1)	16.0 (9.9-26.0)
Cigarette smoking					
No	Reference	1.3 (0.7-2.2)	2.3 (1.3-4.0)	5.5 (3.1-9.7)	10.8 (8.6-17.6)
Yes	0.9 (0.5-1.9)	1.6 (0.9-2.9)	2.7 (1.5-5.0)	6.0 (3.3-10.6)	7.7 (4.5-13.3)
Alcohol use					
No	Reference	1.3 (0.8-2.1)	2.7 (1.7-4.3)	6.1 (3.9-9.7)	10.6 (7.0-16.0)
Yes	1.1 (0.5-2.8)	2.6 (1.3-5.0)	1.7 (0.7-4.4)	5.6 (2.8-11.4)	7.9 (4.5-13.9)

^a Adjusted for age, sex, cigarette smoking, and alcohol consumption except for the stratifying variable

Iloeje UH, et al. *Gastroenterology* 2006;130:678



Long Term Risk - Cirrhosis

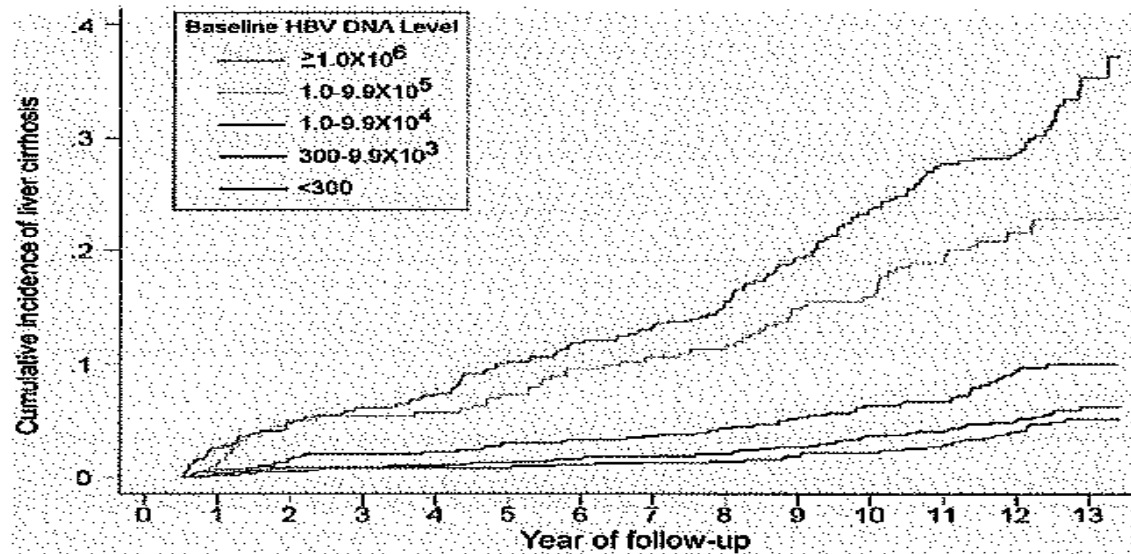


Figure 2. Cumulative incidence of cirrhosis (N = 3582). P value for log-rank test, $< .001$.

Iloeje UH, et al. *Gastroenterology* 2006;130:678



Chronic Hepatitis and LTCI

- LTC Applicants with Chronic Hepatitis B History are Uncommon
- Majority of Applicants with CHB History Acquired Infection During Perinatal Period
- SOA LTC Intercompany Experience Study (11/07)
 - Digestive System Claims Account for 2% LTC Claims
 - Digestive System Claims Costs About 2/3 Average Claim Cost
- Genworth Experience (All Closed Claims as of 1/2011)
 - Cirrhosis Claims (All Causes) Account <1% Claims
 - Cirrhosis Claims Costs About 50% Less Than Average Claim



Case #1

- 56 yo Female of Asian Descent for Well Exam. Recalls Abnormal Hepatitis Test in Past.
- Current Labs:
 - AST 33; ALT 40; Serum Albumin wnl; AFP wnl
 - HBsAg +; HBeAg -; anti-HBeAg +
 - HBV DNA 1,000 IU/ml
 - No Liver Biopsy
- Prior Labs:
 - LFTs 5 Years Ago WNL
- Questions:
 - Risk For Progressive Liver Disease (Low – Medium – High)?
 - What Should Be Done Next?



Case #2

- 62 yo Male – History of Treated Chronic HBV
 - Diagnosed After Abnormal LFTs on Life Insurance Exam
 - History of Multiple Tattoos
- Findings Prior to Treatment
 - AST 97; ALT 125; Serum Albumin wnl; AFP wnl
 - HBsAg +; HBeAg +; anti-HBe Ag –
 - HBV DNA 200,000 IU/ml
 - Liver Biopsy – Grade 2 Inflammation; Stage 1 Fibrosis
- Treated
 - Pegylated Interferon X 48 wks; HBeAg – at 24 and 48 wks
- Current Labs 18 Months Later
 - AST 35; ALT 38; HBsAg +; HBeAg -; anti-HBeAg +
 - HBV DNA Undetectable
 - Liver Biopsy – Grade 1 Inflammation; Stage 1 Fibrosis
- Questions
 - Risk For Progressive Liver Disease (Low – Medium – High)?



Summary

- Hepatitis Immunization Has Decreased the Burden of Chronic Hepatitis B
- For Many, Chronic Hepatitis B is a Chronic Disease
- Oral and Injectable Medications Now Available
- Goal is for Biochemical, Immunologic, Virologic and Histologic Response
- About 25% Will Respond to Treatment
- About 80% of Responders Will Have a Sustained Response
- HBeAg – Disease Has Lower Response to Treatment, Is Prone to Relapses and May Require Long-term Therapy
- Individuals of Asian Descent are Initially “Immune Tolerant”, But Later in Life Often Progress to Chronic Hepatitis
- For Most Individuals, Chronic Hepatitis B is Manageable, But Not Curable