1. A 19 year old Caucasian male is referred to you because he recently developed acute HBV. At the time of diagnosis he was HB surface antigen positive, anti-HB core IgM positive, was icteric with a bilirubin of 6.5 mg/dl and had a serum ALT of 550 IU/l. He has been monitored by his primary care physician for the past 4 months. Serum ALT and bilirubin normalized 2 months ago and HB surface antigen has become undetectable. However, he remains anti-HB surface negative. Which of the following statements is not true of this patient?

a. He is likely to be in the window phase and will eventually develop anti-HB surface with time.
b. Anti-E is likely to be positive.
c. HBV DNA is likely to be negative.
d. He is likely to develop chronic hepatitis B with a mutant form of the virus.
e. He is likely to be anti-HB core positive.

The recommended response is D. This patient has acute HBV and appears to be in the window phase of the natural history of this disease. The time required for anti-HB surface to appear following the resolution of HB surface antigen may take weeks to many months. Since this patient has already normalized serum ALT and bilirubin and has lost HB surface antigen it is very likely he is resolving this infection and does not have chronic HBV with a mutated form of this virus.

2. Which of the following patients are at increased risk to develop fulminant hepatic failure following acute hepatitis A infection:
   a. Women during pregnancy
   b. Patients with chronic hepatitis C virus infection
   c. Exposure to hepatitis A during infancy
   d. Patients with chronic renal failure
   e. Patients with previous exposure to HBV who developed anti-HB surface.

The recommended response is B.

Patients with chronic HCV and likely also patients with chronic liver disease of other etiologies are at increased risk to develop acute liver failure if they develop acute HAV infection. It is therefore recommended that all patients with chronic HCV be vaccinated against HAV.

3. You are referred a 42 year old female recently found to have an elevated ALT by her Oncologist. She was found to have unilateral enlargement of her left parotid gland and a biopsy demonstrated B cell lymphoma. All of the following are likely to be true except.

a. She will likely test positive for anti-HCV.
b. She will likely have cryoglobulimemia.
c. She will likely have proteinurea.
d. She could be treated with peginterferon and ribavirin instead of chemotherapy.
e. She will likely test positive for anti-HB core.

The recommended response is E.

B cell lymphoma is one of the recognized extrahepatic manifestations of chronic HCV. This is typically found in patients with cryoglobulinemia and many of these patients may also have proteinurea secondary to glomerulonephritis. Patients with B cell lymphoma can be treated for HCV with peginterferon and ribavirin. A small case series has demonstrated that this lymphoma will resolve if HCV RNA is eradicated and the patient achieves a sustained virologic response.

4. A 60 year old male with chronic HCV is referred to you for evaluation. He has long standing hypertension, diabetes mellitus type 2, proteinurea and had a myocardial infarction within the past 1 year. He has a long history of depression and was hospitalized for suicidal thoughts shortly after his myocardial infarction. A liver biopsy demonstrates that he has active hepatitis with cirrhosis. Serum ALT is 145 IU/l. All other liver chemistries are normal. Serum HCV RNA is 1 million IU/ml and genotype is 1. Other laboratory studies include a hemoglobin of 12 gms/dl and a platelet count of 50,000. Which of the following in this patient's history is not a contraindication for him to be treated for HCV?

a. Recent myocardial infarction  
b. Hospitalization for severe depression and suicidal thoughts  
c. Diabetes mellitus type 2  
d. Hemoglobin of 12 gm/dl  
e. A platelet count of 50,000

The recommended response is C.

Peginterferon and ribavirin therapy is associated with significant adverse events. As a result it is imperative that factors associated with adverse events to therapy be assessed prior to initiating treatment. One of the major adverse effects is anemia. As a result it is imperative that the hemoglobin be greater than 14 for males and greater than 12 for females prior to initiating treatment. Patients with underlying coronary artery disease are at risk for coronary ischemia if they develop severe anemia and should not be treated if they recently had an MI or if they are having angina. Peginterferon causes both neutropenia and thrombocytopenia. As a result, adequate neutrophils and platelets much be present prior to initiating treatment. Finally, peginterferon may lead to depression and being hospitalized with recent severe depression is a contraindication for treatment.

5. A 35 year old female is found to have chronic HCV and is referred for evaluation. Which of the following laboratory tests is not required to be assessed prior to initiating treatment with peginterferon and ribavirin?
   a. Hemoglobin
   b. Thyroid stimulating factor
   c. Pregnancy test
   d. HCV genotype
   e. Total bilirubin

The recommended response is E.

Prior to starting a patient on peginterferon and ribavirin it is important to assess several factors which are required to define the duration of therapy and to establish a baseline in case toxicities of treatment develop. It is essential to know the HCV genotype as this defines the maximal duration of therapy, 48 weeks for patients with genotypes 1 and 24 weeks for genotypes 2 and 3. Prior to starting the patient on treatment it is essential to define the baseline hemoglobin and ensure this is adequate; since during treatment a mean decline by 2 grams or more is frequently observed. Another frequent toxicity of treatment is thyroid dysfunction. As a result, it is important to assess thyroid function studies at baseline. Since ribavirin is teratogenic, it is essential that all females have a pregnancy test prior to starting HCV treatment.


A 33 year old male with a history of intravenous drug use is hospitalized with acute hepatitis and jaundice. Laboratory studies demonstrate AST 1,500 IU/l, ALT 2000 IU/l, bilirubin 12 mg/dl, INR 1.5, and normal ALP, albumin and bilirubin. An acute hepatitis panel demonstrates the following: anti-HAV IGM negative, HB surface antigen positive, anti-core IgM positive and anti-HCV negative. Over the next 2 days the serum ALT declines to 120 IU/l and the INR normalizes. You discharge the patient but he returns 2 days later with confusion. Serum AST and ALT is now up to 1,500 and 2,000 IU/ml respectively, INR is 4.1 and bilirubin in 22 mg/dl. Which of the following is true of this patients condition?

a. He likely has a relapsing form of acute HAV.
b. He likely has acute liver failure secondary to acute HBV.
c. He likely has acute liver failure secondary to acute HCV superimposed upon chronic HBV infection.
d. He likely has acute liver failure secondary to superinfection with HDV on top of chronic HBV.
e. He likely has acute liver failure secondary to co-infection with HBV and HDV.

The recommended response is E.

This patient has acute infection with HBV indicated by the presence of anti-HB core IgM. This is not acute HAV since the IgM antibody for HAV was negative. Patients with acute HCV may initially be anti-HCV negative. However, the HBV serology indicate that this patient has acute rather than chronic HBV. Patients with acute co-infection with HBV and HDV typically have a bi-modal peak in their clinical presentation. The liver transaminases rise, peak and then decline. It appears that the patient is improving. The patient then develops a second peak in liver transaminases followed by profound liver failure as replication of HDV increases. Such patients have high mortality. However, if they survive they resolve both HBV and HDV infections. In contrast, superinfection with HDV in a patient with chronic HBV rarely causes acute liver failure.


7. You receive a phone call from a Dermatologist who is seeing a patient with porphyria cutanea tarda. The patient is found to have an elevated serum ALT. Which of the following tests would you recommend the Dermatologist order?

a. Anti-HAV IgM  
b. HB surface antigen  
c. anti-HCV  
d. anti-HDV  
e. anti-HEV

The recommended response is C.

Porphyria cutanea tarda (PCT) is a well recognized extrahepatic manifestation of chronic HCV infection. Over half of all patients with PCT have chronic HCV. Other forms of chronic hepatitis can certainly occur in patients with PCT but these are far less likely.

A 25 year old male presents after 1 week of progressive fatigue followed by 2 days of jaundice. Laboratory studies demonstrate serum ALT 225 IU/l, ALP of 330 IU/l and bilirubin of 5.2 mg/dl with normal albumin and INR. A liver ultrasound was normal. He recently returned from a one week vacation in the Caribbean. A positive value for which of the following tests most likely explains this situation?

a. anti-HAV IgM
b. Anti-HB surface
c. anti-HCV
d. anti-HDV
e. anti-HEV

The recommended response is A.

This is a young male who recently returned from an endemic area for viral hepatitis A, B and E. He should therefore be screened for each of these viruses. Anti-HB surface is indicative of prior resolved infection or vaccination and would not be positive in patients with acute HBV. HCV is not typically acquired by traveling unless this patient participated in risk behaviors while on vacation. He could not develop HDV in the absence of either acute or chronic HBV. The most likely scenario is that he developed food borne acute HAV or HEV. Of these, the one most likely to cause a cholestatic hepatitis with elevation in serum ALP is acute HAV.


9. A 33 year old male was found to be anti-HCV positive after attempting to donate blood. He felt well and physical examination was normal. Laboratory studies were all normal. HCV RNA was 1 million copies/ml and genotype was 1A. The patient did not wish to have a liver biopsy or treatment and is seen again, 1 year later after the initial presentation. Repeat laboratory studies remain normal. Repeat HCV RNA is now 1.5 million copies/ml. Which of the following is true?

a. The repeatedly normal serum ALT indicates the patient has mild liver disease without evidence of fibrosis progression.

b. The rise in serum HCV RNA indicates that there has been progression in liver disease over the past 1 year.

c. It is not possible to determine how much fibrosis is present without performing a liver biopsy.

d. Treatment is contraindicated since serum ALT is repeatedly normal.

e. Treatment should not be initiated without first performing a liver biopsy.

The recommended response is C.

This patient has chronic HCV with persistently normal serum ALT. On average, such patients have milder inflammation and less fibrosis than patients with elevated serum ALT. However, approximately 33% patients with persistently normal serum ALT have variable degrees of fibrosis and up to 5% may have cirrhosis. Thus, the presence of a normal serum ALT alone is not a contraindication for HCV treatment. Serum HCV RNA is also not a measure of liver disease severity and generally remains relatively constant over time. It is not necessary to perform a liver biopsy in patients with chronic HCV prior to initiating treatment.

10. A 48 year old Caucasian female presents with severe abdominal pain, fevers and gross hematuria. Laboratory studies demonstrate serum ALT of 223 IU/l, serum albumin of 3.5 mg/dl and creatinine of 3.0 mg/dl. Serum ALP and bilirubin are normal. A CT scan of the abdomen demonstrates numerous aneurysms of the renal and mesenteric arteries. You are called to see her for evaluation. Which of the following statements is most likely to be correct?

a. HCV RNA will be positive.

b. Anti-HAV will be positive.

c. The patient could be treated with peginterferon.

d. Anti-HB core will be positive.

e. anti-HEV will be positive.

The recommended response is D.

This patient appears to have polyarteritis nodosa. This immunologic disorder is associated with acute and chronic HBV. It has not been reported in association with other forms of viral hepatitis or other chronic liver disorders. The disorder is likely secondary to the deposition of virus and immunoglobulin complexes in arterial walls resulting in inflammation and aneurysmal dilation. Treatment with peginterferon is likely not to be effective and may exacerbate this clinical condition since this agent enhances immunologic function.

11. A 35 year old white male who immigrated to the USA from Eastern Europe was found to have chronic HBV and is referred to you for evaluation. He feels well and has no history of acute icteric hepatitis. His physical examination is normal. Laboratory studies demonstrate serum ALT 240 IU/l, with normal ALP, bilirubin, albumin and INR. HB surface antigen is positive, HB E-antigen is positive, anti-E is negative and HBV DNA is 1 million copies/ml. HBV genotype is A. Which of the following characteristics suggests that this patient will have a high rate of seroconversion if treated with peginterferon?

a. The serum ALT.
b. The serum level of HBV DNA
c. Hepatitis B genotype A
d. He is an immigrant from Eastern Europe.
e. He likely acquired HBV as an adult through sexual contacts.

The recommended response is C.

Peginterferon is very effective for treatment of chronic HBV in patients who are E-antigen positive. Approximately 30% of patients develop seroconversion after 48 weeks of treatment. However certain patient characteristics are associated with an even higher rate of seroconversion. These include high levels of serum ALT, low HBV DNA and most importantly genotype A. Of these factors, HBV genotype is likely the strongest predictor of seroconversion. Fifty percent of patients with HBV genotype A will seroconvert during or following treatment with peginterferon. The prevalence of genotype A is greatest in non-Asians. None of the HBV genotypes is associated with a higher rate of seroconversion when utilizing anti-viral agents for treatment.


Marcellin P, Lau GK, Bonino F, et al. Peginterferon alfa-2a alone, lamivudine alone, and the two in


A 42 year old female with chronic HCV is referred for evaluation and possible treatment. Serum ALT is 110 IU/l with normal ALP, bilirubin, albumin and INR. The genotype is 2A and serum level is 2.5 million IU/ml. The patient is adamant that she wants treatment. What type of treatment would you recommend?

a. Peginterferon alfa and ribavirin for 24 weeks
b. Peginterferon alfa and ribavirin for 48 weeks
c. Peginterferon alfa and ribavirin 16 weeks
d. The patient should not be treated until a liver biopsy is performed and liver histologic severity is known
e. Standard interferon and ribavirin for 48 weeks.

The recommended response is A.

Patients with HCV genotype 2 have an approximately 80% chance of achieving SVR when treated for only 24 weeks with either peginterferon or standard interferon for 24 weeks. No studies have demonstrated that a longer duration of therapy is more effective. Recent studies have suggested that a shorter course of peginterferon could possibly be effective but this is not been demonstrated in all studies and the standard of care for such patients continues to be 24 weeks of treatment. A liver biopsy is not absolutely required for a patient to be treated with peginterferon and ribavirin.


13. A 35 year old male with chronic HCV was started on peginterferon alfa and ribavirin. The baseline serum ALT was 75 IU/l with normal ALP, bilirubin, albumin, INR and platelet count of 250,000. HCV genotype was 1A and the serum level of HCV RNA 1.2 million IU/ml. After 4 weeks of treatment HCV RNA had declined to 500,000 IU/ml. After 12 weeks of treatment serum HCV RNA was 300,000 IU/ml. What would you recommend for this patient at this time?

a. The patient has had a continuous stepwise decline in HCV RNA and treatment should be continued for a full 48 weeks.

b. The patient has not achieved an early virologic response and treatment should be terminated.

c. The patient has achieved an early virologic response and treatment should be continued for 48 weeks.

d. The patient has not achieved early virologic response, but has had a marked decline in HCV RNA. Treatment should be continued to 24 weeks and HCV RNA reassessed at that time.

e. The recommended duration of therapy for this patient is 48 weeks. Treatment should be continued regardless of the virologic response to provide the best chance of achieving SVR.

The recommended response is B.

Patients with chronic HCV receiving peginterferon and ribavirin should be carefully monitored at regular intervals. Only those patients who have an early virologic response (EVR) are capable of becoming HCV RNA undetectable and then achieving a sustained virologic response (SVR). An EVR is defined as a 2-log (100 fold) decline in the serum level of HCV RNA from the pre-treatment baseline after 12 weeks of treatment. To achieve an EVR in this case the patient would have to have had a decline in HCV RNA from 1.2 million to 12,000 IU/ml. Since this was not achieved the patient will not achieve SVR and treatment should be discontinued. Continuing treatment beyond...
12 weeks in patients who do not achieve EVR will not lower HCV RNA to undetectable levels. Although it is recommended that patients with genotype 1 be treated for 48 weeks to have the best chance of achieving SVR, this can only be achieved in those patients who first achieve EVR and then become HCV RNA undetectable by week 24.


A 19 year old female is referred to you because of acute icteric hepatitis. She notes that this first developed about 2 weeks ago and is associated with fatigue, but denies arthralgias, myalgias, ascites, edema or problems with short term memory. She has not traveled outside the United States. She has had a single sexual partner for the past 6 months and utilizes oral contraceptives for birth control. Serum AST and ALT by the referring physician 1 week ago were 1,000 and 1,500 IU/l and bilirubin was 10 mg/dl. On physical examination she is icteric and there is mild tender hepatomegally without acites. The rest of the physical examination is normal. You obtain the following laboratory tests: AST 900 IU/l, ALT 1,000 IU/l, bilirubin 12 mg/dl, ALP is normal, albumin 3.8 gm/dl and INR 1.8, HB surface antigen positive, anti-HB core IgM positive, anti-HCV negative and anti-HAV IgM negative. Which of the following statements are correct?

a. The patient is at high risk for development of chronic hepatitis and should be started on an anti-viral agent (either lamivudine, adefovir or entecovir).

b. The patient is at high risk for development of chronic hepatitis and should be started on peginterferon.

c. The patient is at high risk to develop chronic hepatitis and should be monitored for 6 months and then started on peginterferon.

d. The patient is at low risk for development of chronic hepatitis but should be monitored until resolution occurs.

e. The patient is at low risk to develop chronic hepatitis, will resolve the acute infection and therefore does not need further monitoring.

The recommended response is D.

This patient has acute icteric HBV with preserved hepatic function. There is no evidence of acute liver failure. The likelihood that an adult with acute icteric HBV will completely resolve this infection and develop anti-HBs surface exceeds 90%. Those adults at greatest risk to develop chronic HBV are generally asymptomatic and anicteric during the acute infection. None of the approved
treatments for HBV are indicated in patients with acute disease since the resolution rate is so high.

All patients with acute HBV should be monitored until the episode resolves and the patient has developed protective antibodies. Peginterferon is an effective therapy for patients with chronic HBV. However, since this patient had acute icteric hepatitis and is likely to resolve her infection and develop protective antibodies this treatment is not required.


15. A 44 year old Asian male is referred to you for ongoing management of chronic HBV. He was born in Korea but immigrated to the United States when he was 18 years of age. He was found to be HB surface antigen positive and started on lamivudine 100 mg daily. Laboratory studies at the time of diagnosis and after 1 year of treatment are listed below. What would you do at this time?

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>After 1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT (IU/l)</td>
<td>230 IU/l</td>
<td>23 IU/l</td>
</tr>
<tr>
<td>E-antigen</td>
<td>positive</td>
<td>positive</td>
</tr>
<tr>
<td>anti-E</td>
<td>negative</td>
<td>negative</td>
</tr>
<tr>
<td>HBV DNA</td>
<td>8 million copies/ml</td>
<td>undetectable</td>
</tr>
</tbody>
</table>

a. Continue lamivudine.

b. Add adefovir dipivoxil to limit the development of resistance.

c. Add peginterferon and treat with both drugs for 48 weeks.

d. Stop lamivudine since he is HBV DNA undetectable.

e. Switch to entecovir since he has evidence of resistance to lamivudine.

The recommended response is A.

This patient has E-antigen positive chronic HBV. The primary goal when treating such a patient is seroconversion; loss of E-antigen and development of anti-E. When treating HBV with anti-viral agents, either lamivudine, adefovir dipivoxil or entecovir, this treatment should be continued until the patient has lost E-antigen and developed anti-E. Many experts suggest that treatment should be continued for 6 months after seroconversion and development of anti-E to limit the chance of reactivation. Discontinuing treatment prior to seroconversion, even after the patient has become HBV DNA undetectable, as in this case, will result in reactivation. In some cases reactivation can be severe and precipitate acute hepatic failure. Lamivudine has the highest rate of resistance of all
the anti-viral agents currently available. However, once patients are HBV DNA negative the rate of resistance is low. Thus, there is no real need to switch to an alternative agent in this patient at this time. If HBV DNA was still detectable after 1 year, switching to an alternate anti-viral agent would have been a reasonable choice. The data does not suggest that utilizing peginterferon in combination with an anti-viral agent will enhance the effectiveness of treatment and this should not be considered.


A 55 year old male is found to have chronic HCV. Serum ALT is 85 IU/ml with normal ALP, bilirubin, albumin, INR and a platelet count of 300,000/cc. HCV genotype is 1A and serum HCV RNA 800,000 IU/ml. Liver biopsy demonstrated active hepatitis with portal fibrosis. Serologic studies demonstrate anti-HAV total negative, HB surface antigen negative, anti-HB-core positive and anti-HB-surface positive. Prior to considering the patient for HCV treatment, which of the following would you recommend?

a. Upper endoscopy to exclude varicies.
b. A liver ultrasound to exclude hepatocellular carcinoma.
c. Vaccination for hepatitis A.
d. Vaccination for hepatitis B.
e. Screening of the patient’s spouse or sexual partner to ensure he does not get reinfected during treatment.

The recommended response is C.

The patient has chronic HCV with only portal fibrosis. Patients with chronic HCV are not at increased risk to develop HCC until they develop cirrhosis. Thus, although it would not be unreasonable to perform an ultrasound of the liver to exclude cysts, hemangiomas or other lesions prior to performing a liver biopsy, it is not necessary to screen this patient for HCC. Similarly, since the primary cause of varicies in patients with chronic HCV is portal hypertension secondary to cirrhosis and there is no evidence for this, an upper endoscopy does not need to be performed. Patients with chronic HCV are at increased risk to develop acute liver failure when exposed to either HAV or HBV. As a result, it is recommended that all patients with chronic HCV be vaccinated for these viruses if not previously exposed. This patient has not been exposed to HAV since anti-HAV total is not detectable. However, he has been previously exposed to HBV and already has protective antibodies against this virus. Therefore this patient does not require vaccination against HBV. The risk of sexually transmitting HCV is very rare. Thus, while it would be reasonable to
recommend that this patient’s spouse/sexual partner be tested for HCV the results of this do not preclude treatment.


A 66 year old Asian male is referred to you for evaluation. The physical examination is significant for spider angiomata and he is mildly icteric. There is no ascites or lower edema and the mental status is normal. Laboratory studies demonstrate ALT 45 IU/l, bilirubin 3.5 mg/dl, albumin 2.2 gm/dl, INR 1.5, platelet count 90,000 and AFP 11 mg/ml. Serologic studies demonstrate HB surface antigen positive, E-antigen negative, anti-E positive and HBV DNA of 10,000 copies/ml. Which one of the following would you not recommend?

a. Initiate therapy with an anti-viral agent (lamivudine, adefovir or entecovir).
b. Evaluate the patient for liver transplantation.
c. Initiate treatment with peginterferon.
d. Ultrasound examination of the liver to screen for hepatocellular carcinoma.
e. Screen all other family members for hepatitis B.

The recommended response is C.

This patient has evidence of chronic hepatitis B based upon the presence of HB surface antigen. Even though you are not provided with an anti-HBV core IGM, the presence of anti-E, his age and race suggests that his initial exposure was many years ago and therefore this is chronic not acute HBV. This patient also has clinical and laboratory evidence of cirrhosis, spider angiomata, a low serum albumin and thrombocytopenia. His HBV DNA is low suggesting that he has inactive disease. However, given that he has cirrhosis it would be recommended that he be treated regardless of the serum HBV DNA level. Patients with cirrhosis are best treated with anti-viral agents since they do not lead to hepatic decompensation. In contrast, peginterferon is generally not recommended for persons with cirrhosis, especially decompensated cirrhosis, since this treatment is at times associated with a flare in the hepatitis and may precipitate hepatic decompensation. Since the patient has evidence of cirrhosis with a decline in hepatic synthetic function it is very reasonable to consider this patient a candidate for liver transplantation. Patients with long standing chronic HBV are also at risk for HCC and should be screened for this with an
ultrasound of the liver. It would be inappropriate not to offer this patient treatment with an anti-viral agent given the presence of cirrhosis even though the level of HBV DNA is low.
