

## Đáp Án Đề Thi Gan Mật

### 1/ Answer e.

This patient has inactive chronic hepatitis B characterized by the presence of hepatitis B surface antigen, normal liver enzyme levels, and HBV DNA level  $<20,000$  IU/mL. She is at risk of transmitting infection, and her children should receive hepatitis B immune globulin and hepatitis B vaccination at birth. Patients are generally not treated for hepatitis B unless there is disease activity, including abnormal aminotransferase levels and HBV DNA level  $>20,000$  IU/mL. EGD is not necessary unless there is evidence of cirrhosis.

### 2/ Answer b.

Patients with cirrhosis and gastrointestinal bleeding are at high risk of infection and should receive prophylactic norfloxacin for 7 days, even if there is no ascites. A TIPS would be necessary only if there is refractory bleeding. Although the hemoglobin level should be carefully monitored, the patient is currently stable and does not need transfusion now. Excessive transfusion can precipitate recurrence of bleeding and fluid overload. Fresh frozen plasma is also not necessary given the relatively normal INR. Long-term pegylated interferon for patients who have no response to treatment should be considered experimental and is not routinely given.

### 3/ The answer is B.

Hepatic adenomas are benign tumors of the liver found in women in the third and fourth decades. Hormones are thought to play an essential pathophysiologic role. The risk of adenomas is increased among those taking oral contraceptives, anabolic steroids, and exogenous androgens. These adenomas typically occur in the right lobe and are often asymptomatic and are discovered incidentally. Clinical features may include pain or a palpable mass. Diagnosis is usually made by a combination of modalities, including ultrasound, CT, MRI, and nuclear medicine. The risk of malignant transformation is low. Surveillance is recommended for asymptomatic small lesions. However, since this patient has significant pain, an intervention is necessary. In light of the relationship with hormones and the low risk of malignant transformation, the first option would be discontinuation of oral contraceptive therapy and follow-up in 4 to 6 weeks. Tumors that do not shrink after discontinuation of oral contraceptives may require surgical excision. RFA has no established role, and biopsy is not indicated as the clinical picture is highly suggestive of a benign lesion. Advice should be given to patients with large adenomas that pregnancy may exacerbate symptoms and promote hemorrhage.

### 4/ Answer b: Continue lamivudine and add adefovir

The general principle of management of hepatitis B virus (HBV) antiviral drug resistance is to add a second drug that is not cross-resistant with the first drug (eg, add a nucleotide drug such as adefovir [or tenofovir] when resistance to a nucleoside agent such as lamivudine, telbivudine, or entecavir is detected). Thus, the use of entecavir or telbivudine for lamivudine resistance is not an appropriate treatment strategy. The opposite concept applies to the patient with adefovir resistance (ie, add a nucleoside agent). The strategy of *adding* vs *switching* to a second drug is supported by studies showing that the rate of subsequent adefovir resistance is considerably higher with the switch strategy in the setting of preexisting lamivudine resistance.

### 5/ Answer d: Serum HBV DNA level of 4000 IU/mL after 24 weeks of therapy

An inadequate virologic response, according to the published "roadmap" concept for the on-treatment management of chronic hepatitis B, is defined as a serum HBV DNA of  $\geq 2000$  IU/mL after 24 weeks

of therapy. These patients have failed therapy and need to be changed to an alternative regimen, with either a different drug that is more potent and not cross-resistant or the addition of a second drug.

6/ **Answer is: a)** Increased

ETV-901 is a long-term extension trial in which patients from study ETV-022 (HBeAg-positive patients) and from study ETV-027 (HBeAg-negative patients), both placebo-controlled studies, could continue taking entecavir. Data by Han and colleagues, presented at AASLD 2007, evaluated 146 HBeAg-positive patients from ETV-901 who had a treatment gap of 35 days or fewer between finishing in ETV-022 and starting in ETV-901 (Abstract/Poster 938). At week 48, 55% of patients had achieved HBV DNA levels of <300 copies/mL. The percentages at weeks 96, 144, and 192 were 83%, 89%, and 91%, respectively.

7/ **Answer c:** 12-month mortality

Zapater and colleagues reported on the measurement of a novel marker, bacterial DNA, in ascites fluid as a predictor of survival in cirrhotic patients with noninfected ascites. They analyzed the ascites fluid from 156 patients with sterile ascites, 48 of whom had bacterial DNA detected by polymerase chain reaction analysis. The presence of bacterial DNA (mostly *Escherichia coli*) was significantly associated with 12-month mortality (ie, was an indicator of poor prognosis), but surprisingly, the DNA-containing group did not have a higher incidence of spontaneous bacterial peritonitis.

8/ **Answer c:** 80%

In a study by Lampertico and colleagues, 145 chronic hepatitis B patients with documented lamivudine resistance had adefovir added to their treatment regimen and were monitored for a median of 42 months. Overall, 80% of patients became HBV DNA negative by year 3; 20% remained viremic despite combination therapy. No patient experienced virologic breakthrough (defined as > 1 log<sub>10</sub> increase in serum HBV DNA over on-treatment nadir).

9/ **answer c;** Propranolol

Although studies reported at AASLD 2007 have shown carvediol to be beneficial in the primary prophylaxis of esophageal varices, the standard nonselective beta-blockers, such as propranolol, have been reproducibly shown to be the standard of care in this setting.

10/ **Answer d:** Ultrasound surveillance every 6 months

This patient is at significant risk for HCC and meets guidelines for surveillance. For individuals with small tumors and intact hepatic function without portal hypertension, resection provides nearly equivalent outcomes as orthotopic liver transplantation, although there is an increased recurrence rate. Thus, if technically feasible, resection is favored over transplantation for these patients. Therefore, he has no indications for liver transplantation given his intact hepatic function. Maintenance pegylated interferon appears to be ineffective.

11/ **b**

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**B Autoimmune hepatitis**

Development of **primary biliary cirrhosis (PBC)** is associated with increased serum levels of alkaline phosphatase and serum gamma glutamyl transpeptidase (due to biliary ducts obstruction), as well as with elevated serum IgM levels. Existence of normal alkaline and gamma glutamyl transpeptidase levels is a strong diagnostic argument against diagnosis of PBC. Since the levels of both of those enzymes and IgM are normal in the presented patient, it is unlikely that she suffers from PBC. Although antimitochondrial antibody is present in almost all PBC patients, it is not specific for this disease, and may be present in low titer in patients with autoimmune hepatitis as well. Therefore, it is unlikely that the presented patient suffers from primary biliary cirrhosis.

**Secondary biliary cirrhosis** appears as the result of long-lasting cholestasis. However, presence of normal alkaline phosphatase and gamma glutamyl transpeptidase levels is a diagnostic argument against existence of cholestasis. Since the presented patient underwent cholecystectomy ten months before the appearance of symptoms, previous existence of gallstones or choledocholithiasis cannot be related to her present disease. Therefore, the possibility of **secondary biliary cirrhosis** has to be ruled out.

The presented patient takes alcohol for only six weeks, which is a relatively short period for the development of serious liver damage. Signs of liver disease (jaundice and malaise) appeared before the misuse of alcohol; therefore, alcohol intake cannot be blamed for the appearance of liver disease. In addition, the existence of elevated gamma globulin level points to the presence of chronic, rather than acute, liver disease. In other words, the possibility of **acute alcoholic hepatitis** has to be excluded in her case.

The existence of anti-HBs and anti-Hbc antibodies in the patient's serum shows that she had hepatitis B once in her lifetime. However, since HBsAg and hepatitis B virus DNA are absent in her serum, it is clear that she has no active viral infection. Therefore, it is unlikely that she has **chronic B hepatitis** now.

The appearance of various autoantibodies (including antinuclear antibody) that are accompanied with clinical and laboratory signs of liver dysfunction, characterize **autoimmune hepatitis**. Elevated levels of immunoglobulins, including IgG are also present and low titer of antimitochondrial antibody in the patient's serum may also exist. Since all of the described abnormalities exist in the presented case, she probably suffers from **chronic autoimmune hepatitis**.

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12/c

Answer: Advanced patient age

Patients infected with HCV genotype 3 have an 80% or better response rate to treatment with pegylated interferon and ribavirin. However, the reason the remaining 20% of patients fail to respond is often not clear. In a study involving 34 treatment-naive patients with HCV genotype 3 infection -- 16 of whom were nonresponders to treatment -- sex; age; body weight; comorbidities, such as diabetes mellitus; and baseline HCV RNA and ALT levels were evaluated. When studied by univariate and multivariate analysis, only age remained as a factor associated with nonresponse to therapy (ie, therapy response is negatively affected by increasing age).

13/C

Courtesy of Health Professions Division Library/ EXPLANATION

**C Infection with HBV2 mutant**

After an episode of acute hepatitis B, a so-called **"healthy" carrier** state frequently develops. However, since in some cases hepatitis B infection may run a prolonged course, it is an accepted medical standard that only those patients, who do not eliminate HBsAg six months after the onset of infection, may be considered chronic carriers. Since our patient developed hepatitis B infection five months ago, he still cannot be considered as a chronic carrier.

Acute infection with hepatitis B virus may lead to the **development of chronic B hepatitis**. However, due to a short time period (less than six months) which has passed from the disease onset, as well as due to the absence of HBeAg, which is the marker of an intensive replication of the virus and tendency towards chronicity, diagnosis of chronic B hepatitis cannot be established.

**Infection with surface region mutant** is frequent in people who received the hepatitis B vaccine. It is the result of mutation in surface region, which enables mutant virus to escape vaccine-induced immune protection. However, patients infected with this sort of mutant, develop positive anti-HBc antibodies as well as positive HBeAg and anti-HBe antibodies. Since no anti-HBc, HBeAg or anti-HBe antibodies are present in serum of presented patient, it is unlikely that he is infected with this sort of mutant.

**Infection with pre-core region mutant** is characterized with present HBsAg and anti-HBc antibodies, but HBeAg is absent in patient's serum due to a mutation in pre-core region of the virus which causes decreased release of HBeAg. Infection with this sort of mutant may be excluded, because the serum of our patient is absent not only HBeAg, but also anti-HBc antibodies.

**Infection with HBV2 mutant** is characterized with presence of HBsAg, but absence of HBeAg as well as the absence of anti-HBc antibodies due to a mutation of the core region of virus that helps virus to escape immune response. In addition, HBV DNA is frequently undetectable, and all the above-mentioned characteristics are present in this case.

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14/ c

**C** The patient is at risk for development of chronic hepatitis

**As with this patient, at least half of patients infected with hepatitis C develop chronic hepatitis.** It is usually acquired by parenteral route of infection. Testing for HCV antibody has eliminated many, but not all, cases of transfusion-associated hepatitis from HCV. An antigen test is not yet available.

Viral hepatitis is a risk factor, and the most common antecedent to hepatocellular carcinoma. Though viral hepatitis can be a sexually transmitted disease, the incubation period for hepatitis C is similar to B, which is months. Despite advanced testing schemes, cases of hepatitis C still occur from blood transfusion. The findings suggest chronic hepatitis C infection, which will not generally resolve quickly and spontaneously.

15/ b,d

The phase 3 GLOBE trial evaluated the safety and efficacy of telbivudine in both HBeAg-positive and HBeAg-negative patients with chronic HBV. Zeuzem and colleagues performed a retrospective analysis to identify baseline and early on-treatment variables that were predictive of telbivudine efficacy at week 104 (AASLD 2007. Abstract/Poster 994).

For HBeAg-positive patients, predictors of long-term treatment success included baseline HBV DNA  $<10^9$  copies/mL, ALT  $\geq 2 \times$  ULN at baseline, and undetectable HBV DNA at week 24.