**Question # 25**

A 56-year-old male patient has diabetic nephropathy (serum creatinine = 1.92 mg/dL) and newly diagnosed HIV infection (CD4 = 250 cells/mm³, viral load = 75,000 copies/mL).

After consultation with the nephrologist and pharmacist, you wish to start him on efavirenz + abacavir/lamivudine as a once daily regimen.

Which of the following laboratory tests would be useful in maximizing the safety of this regimen?

A. CYP2C9  
B. HLA-B*5701  
C. Trofile  
D. Urine for total protein  
E. Serum albumen

**Correct answer: B**

**Rationale:**

HLA-B*5701 allele is a risk factor for this reaction and should be tested for prior to using abacavir. If testing is not feasible, abacavir can still be given with appropriate patient counseling and close monitoring. Abacavir may cause a serious and even life threatening hypersensitivity reaction that occurs within the first few weeks of therapy (median time = 11 days), which may present with high fever, skin rash, flu-like syndrome, gastrointestinal symptoms (nausea, vomiting, abdominal pain, diarrhea,) and respiratory symptoms. These reactions generally subside upon discontinuation of abacavir, but may recur and with more serious symptoms and outcomes if the patients are rechallenged with abacavir later on.

Approximately 8% of caucasians, 2% of blacks, and very few Asians will be screened out by this testing.
**Question # 26**

A 40-year-old white male was switched to a darunavir/ritonavir/enfuvirtide/tenofovir and emtricitabine regimen, secondary to virologic failure and multiple PI mutations including I50L. He presents to the clinic 6 month after the switch for a routine evaluation.

Current CD4 = 350 and VL = <50 copies

Lipids drawn during the evaluation reveal
- Total cholesterol of 260
- LDL 130
- HDL 35
- Triglycerides 1200

What is the most appropriate management for his hypertriglyceridemia?

A. Switch patient to nevirapine-based regimen.
B. Switch patient to an atazanavir-based regimen.
C. Increase exercise regimen.
D. Fenofibrate
E. Fat-free diet

**Correct answer: D**

**Rationale:**

This patient should be started on fenofibrate to reduce his triglycerides.

He should not be put on atazanavir based regimen because of his 150 L mutation, which is an important part of this question. Atazanavir based regimens are attractive for patients with lipid abnormalities. For the boards, however, you should recognize that I50L mutation is associated with non-response to atazanavir. This patient needs some other drug, not atazanavir.

This lipid profile reveals a predominant hypertriglyceridemia. Statins are not the preferred agents for the treatment of predominant hypertriglyceridemia. Fenofibrate would be reasonable choices, so D is a good answer. Niacin is usually used as a second line drug for triglycerides if fibrates are not effective or not tolerated.

An important fact not tested here: despite the lack of Cyp 3A4 metabolism, the use of pravastatin with darunavir results in significant increases in the pravastatin AUC and is not recommended for concurrent use.
Question # 27

A 25-year-old woman in Dallas, Texas has come to the hospital for antenatal care. She reports no prior illnesses and has never been tested for HIV.

Her lab report is as follows:

- Pregnancy test: Positive
- Ultrasound: Normal 16 week gestation
- CD4 Count: 490 cells/μL
- Viral Load: 200,000
- CBC and Chem 12: Unremarkable

The obstetrician seeks your advice.

You would recommend:
- A. Elective caesarian section regardless of viral load on antiretroviral therapy
- B. Single dose nevirapine at time of delivery for mother and single dose for infant within 2 hours of delivery but no other antiretroviral regimen during pregnancy.
- C. Lopinavir-ritonavir, tenofovir, lamivudine to start immediately
- D. Efavirenz and tenofovir-emtricitabine (Truvada) to start immediately.

Correct answer: C

Rationale:

This woman requires ART to benefit her fetus and to benefit her own health.

Most clinicians would also consider it imperative to start her on ART to benefit her since her CD4 count is below 500 cells.

Since efavirenz is contraindicated during the first trimester, lopinavir ritonavir containing regimens would be appropriate and thus C is the best answer.

Single dose nevirapine is indicated only in resource limited settings where combination therapy is not feasible. There is no role for single drug therapy in the United States.

C-Section would pose no benefit if the mother has a good response to ART and has a viral load less than 50 in the third trimester. An elective C section is indicated if the mother cannot obtain a viral load less than 1000 copies on ART prior to going into labor.

Note that in pregnancy, CD4 absolute counts are likely to be lower than prepregnancy. The percentage is a better reflection of immune competence. This decrease in absolute CD4 count is probably due to altered blood volume and volume of distribution.
Question # 28

A 53-year-old HIV-infected male on a long-term first regimen of efavirenz-zidovudine-lamivudine, with excellent virologic control (VL less than 50 copies, CD4=600 cells), was admitted to the trauma center after a gunshot wound to his abdomen. His antiretroviral drugs were not started in the hospital since he was taking nothing by mouth for most of the three weeks he was there.

His efavirenz-zidovudine-lamivudine were restarted at discharge. Three months after discharge from the hospital, he was eating well and regaining his weight and had the following lab results: viral load of 7,500 copies/mL, and CD4 count of 495 cells/mm3. He stated that he has been adherent to all his antiretroviral drugs since discharge.

Which of the following resistance mutation(s) are most likely to be detected in this patient on his current regimen?

A. T215Y  
B. L90M  
C. K103N +/- M184V  
D. K65R  
E. Q148R

Correct answer: C

Rationale:

Antiretroviral treatment interruption is generally not recommended, but in this patient there was no choice but to stop them suddenly at the time of his abdominal trauma. The problem with this patient was that his efavirenz has a much longer half life (40-55 hours) than his nucleosides (intracellular half lives are 7-22 hours). Thus, when first in the hospital he was on monotherapy, effectively, for much of the first week until the serum efavirenz levels reached zero.

Since both efavirenz and lamivudine have low barriers to resistance, in this patient K103N (efavirenz) and M184V (lamivudine) were the most likely mutations to emerge.

You should know what the other mutations listed are: L90M is a PI mutation—there is no reason for this patient have this since he never received these drugs, and presumably was not infected with a primary resistant strain.

K65R is the signature tenofovir mutation, but again this patient was not known to have been exposed to this drug. Q148R is a key raltegravir mutation.
Question # 29

A 25-year-old HIV infected man is seen for routine HIV care. He has received tenofovir, emtricitabine, and efavirenz for the past year but has a history of a poor response and currently has a viral load that is 10,000 copies on repeated determinations despite his assurances of adherence.

Resistance profile on his current regimen includes:
- Nucleoside: M184V
- Non nucleoside K103N
- Phenotype: susceptible to all protease inhibitors, AZT, D4T

He is hepatitis B seropositive (HBsAg positive).

The most prudent management strategy for this patient would be:

A. Discontinue his current regimen and repeat the genotype after he has been off antiretrovirals for 4 weeks.
B. Change his regimen to Abacavir, Lopinavir-Ritonavir, and Raltegravir.
C. Change his regimen to Zidovudine, Lamivudine, Lopinavir-Ritonavir.
D. Change his regimen to Tenofovir, FTC, Lopinavir-Ritonavir.
E. Change his regimen to Abacavir, Lamivudine, Lopinavir-Ritonavir.

Correct answer: D

Rationale:

If this patient is started on an effective antiretroviral regimen and has a substantial rise in CD4 and fall in VL, a hepatitis B flare would be a major concern. Thus, prudent management would dictate that he receive at least two active drugs against hepatitis B.

Choices B, C and E might be fine for his HIV, but would not provide activity against HBV to prevent a flare of HBV.

A is incorrect: resistance testing should always be done while the patient is on the current regimen. The longer a patient is off the regimen, the more likely wild type virus will emerge on testing, obscuring the archived resistant virus that well reemerge when there is selective drug pressure of a new regimen.

The following drugs have Hepatitis B activity: Emtricitabine, Lamivudine, Tenofovir, Adefovir, Entecavir, or Telbivudine. At least two drugs with HBV activity should be used concurrently to reduce the likelihood of resistance.
Question # 30

A 32-year-old female presents to the clinic for evaluation. She has been on combivir and efavirenz for 18 months. She admits to intermittent non-compliance and at this visit has a CD4 count of 198 and a viral load of 27,500 copies.

A genotype is done and reveals the following mutations:

Nucleosides: M41L and T215Y

Non nucleosides: K103N

Which of the following regimens would be the best choice for this patient?

A. Tenofovir, FTC, efavirenz
B. AZT, 3TC, atazanavir, ritonavir
C. Tenofovir, FTC, atazanavir, ritonavir
D. Abacavir, 3TC, efavirenz

Correct answer: C

Rationale:
The K103N mutation rules out efavirenz as a viable option, and thus A and C are incorrect. Thymidine analog mutations (TAMS) such as M41L and T215Y confer high level resistance to AZT, and multiple TAMS may confer low level resistance to Tenofovir.

Thus the best regimen for this patient must not contain efavirenz, and should contain tenofovir in preference to zidovudine, which leaves C as the best answer.
Question # 31

A 53-year-old man with a 15-year history of various regimens of antiretroviral therapy is tested by Trofile assay to determine the suitability of maraviroc therapy. His CD4 count = 20 cells. He has 100% R5 virus.

He is started on a maraviroc containing regimen, but 3 months later he is still viremic. Repeat Trofile shows 100% X4 virus.

Which of the following is most correct:

A. Late stage HIV infection is characterized by X4-tropic virus only. The original Trofile assay was erroneous.
B. Late stage HIV infection is characterized by R5-tropic virus only, The original Trofile was correct but the repeat is erroneous.
C. The original Trofile was likely correct and Maraviroc therapy resulted in emergence of X4 tropic virus that was present at low levels prior to initiating the maraviroc.
D. If the initial test was correct that 100% of virus was R5, then the resulting resistant virus should be mutant R5, not X4.

Correct answer: C

Rationale:

When chronically infected patients are tested, they may have X4 or R5 coreceptor virus, or they may have both viruses. HIV-1 enters cells by binding to the CD4 receptor and to either the X4 or R5 coreceptor. In late stage HIV-1 infection, approximately 50% of all infections are characterized by HIV using X4 coreceptor, and the remaining 50% of infections use either R5 coreceptor or a combination of R5 and X4 coreceptors. Thus both A and B are wrong.

Maraviroc is a coreceptor inhibitor that is only active against HIV-1 utilizing the R5 coreceptor. Resistance to maraviroc with emergence of new resistance mutations in R5 develops, but very slowly. In most cases rebound viremia is attributable to emergence of X4 tropic virus that was present in low levels prior to starting coreceptor inhibitor. Thus D is wrong and C is correct.
Question # 32

A 22-year-old male computer engineer was found to be HIV-infected during a routine ER visit for minor trauma. (CD4 count = 450 cells/µL, VL = 50,000 copies/µL).

He was started on efavirenz, tenofovir, and emtricitabine.

His most recent sexual contact was 90 days ago with an anonymous partner. He was RPR negative at that time and again when he started ART.

Nine days after starting therapy, he developed a mildly itchy rash over his trunk, face and extremities including palms and soles. He has no blistering lesions and no lesions on his oral mucosa.

The best advice for this patient is:

A. Continue the ART regimen.
B. Switch the efavirenz to lopinavir-ritonavir.
C. Switch tenofovir-emtricitabine to zidovudine-lamivudine.
D. Treat with benzathine penicillin.

Correct answer: A

Rationale:
This pruritic rash is most likely due to efavirenz. Rashes due to efavirenz are common, usually mild and self-limiting, and occur at a median time of 9 days after starting therapy. Progression to Stevens-Johnson is extremely uncommon with efavirenz, and this patient has no such suggestive findings.

Rashes to tenofovir and emtricitabine are less common.

A rash on the palms and soles could be syphilis, but the pruritus and the two negative RPRs make this less likely. Manifestations of syphilis occur at a median time of 21 days, and thus this would be unusually late, occurring 90 days after his last exposure.
Question # 33

A 42-year-old male with HIV (initial CD 4= 10, initial viral load -500,000 copies but current CD4 =50, VL <50 on darunavir/ritonavir, tenofovir, emtricitabine started at another clinic 1 month ago) presents with 2 months of apathy, mild memory loss, bilateral hand tremors , but no fever.

Evaluation reveals of negative serum IgG for toxoplasma and CMV and negative RPR.

MRI is shown.

LP reveals 20 wbc (100% lymphocytes), protein 110mg/dl, glucose 80 g/dl), crypt anitgen negative. VDRL negative and toxoplasma PCR negative.

The most like cause of this patient's cognitive decline is:

A. JC encephalitis
B. Progressive multifocal leukoencephalopathy
C. Darunavir toxicity
D. HIV encephalopathy
E. HHV 8 encephalopathy

Correct answer: D

Rationale:
This patient has classic HIV dementia with mild ventricular enlargement and periventricular enhancement. The triad of cognitive loss (memory, concentration, executive function), behavioral issues (apathy) and motor abnormalities (tremor) are typical. This patient has HIV encephalopathy.

CMV encephalopathy is generally more acute, is associated with neutrophils in the CSF in some cases, and would be unlikely to occur in a patient who is responding to ART, and who has a negative CMV IgG antibody. Periventricular enhancement does occur with CMV encephalitis, however.
HHV 8 does not cause encephalopathy.

HHV 6 has occasionally been associated with an acute or subacute encephalopathy, but that was not offered as an answer.

JC encephalitis, or Progressive Multifocal leukoencephalopathy usually manifests with multiple focal white matter lesions. A CSF JC PCR would confirm this diagnosis if the clinical history and MRI were compatible.

With negative serum RPR, CNS syphilis is not likely in a patient of this age. The negative CSF VDRL does not, however, rule out neurosyphilis.
A 47-year-old male with lymphoma has been hospitalized for an allogeneic myeloablative stem cell transplant with a conditioning regimen of cyclophosphamide and total body irradiation. He is now 35 days post-transplant, receiving cyclosporine, mycophenolate, trimethoprim-sulfamethoxazole, fluconazole, and acyclovir, and has received several courses of pulse steroids for graft-versus-host disease. His white blood count is 3500 cells/µL.

Sixty days post transplant, he developed gross hematuria with extreme pain on urination and he is passing clots of blood in his urine. His urinalysis shows rare leukocytes, the nitrate test is negative and his urine culture is negative for routine bacterial and fungal pathogens.

His cytology for BK virus is negative, as is BK PCR of his blood and urine.

Which one of the following would be the most likely cause of hemorrhagic cystitis in this patient?

A. Cyclosporine  
B. Herpesvirus type  
C. JC virus  
D. Adenovirus  
E. Cytomegalovirus

Correct answer: D  
Rationale:
Adenovirus and BK virus are important cause of hemorrhagic cystitis in this patient population, as is cyclophosphamide (cytoxan). In this case, BK was ruled out by the PCR tests in the stem cell and cytoxan is not offered as an answer. Hematuria due to cytoxan (cyclophosphamide) usually starts within 48 hrs of the dose, making that unlikely in this case. Radiation also causes hemorrhagic cystitis. Beta lactam drugs rarely do this: this is probably too obscure for the exam.

Adenovirus is an important cause of hemorrhagic cystitis which can be latent in an HSCT recipient from a remote infection and reactivate during periods of intense immunosuppression. Active adenovirus infection may be asymptomatic and detected only by PCR of peripheral blood, or may present clinically as hepatitis, or diffuse pneumonia or cystitis.

Diffuse cystitis may be so severe that the patient has urethral obstruction from blood clots and such intense pain on voiding that narcotics may be required. There is no specific therapy for adenovirus: some clinicians might use cidofovir, but the most plausible strategy at this point for therapy is to minimize the degree of immunosuppression, which can be a complicated challenge.

CMV, HSV, JC and cyclosporine do not cause hematuria. Cyclosporine causes renal dysfunction; HSV can cause vaginitis and cause dyuria and pyria, and CMV can occasionally cause glomeular disease.

This patient was BK negative. However, BK, a polyoma virus may reactivate under the same circumstances as adenovirus and appear in the urine in high copy number. Although BK may cause renal tubular damage in transplanted kidneys, the role of this virus as a cause of hematuria remains a subject of diagnostic debate: some cystitis and hematuria is clearly due to BK virus, but how to
recognize such cases without biopsy or cytology is difficult because BK viruria in high quantities may be present without cystitis.
Question # 35

A 55-year-old CMV seronegative Caucasian woman with type 1 diabetes mellitus and end stage renal disease received a cadaveric renal allograft from a CMV positive donor six months prior and now presents with decreasing renal function despite increased immunosuppression with tacrolimus and prednisone given for suspected graft rejection. Ultrasound did not show obstruction of the implanted kidney. You are consulted about possible infectious causes of renal failure. She is afebrile and routine urinalysis with bacterial culture is unremarkable.

Your best option to establish the cause of the renal failure is which of the following:

A. Urine viral culture  
B. Urine cytology  
C. Renal biopsy  
D. Blood for quantitative CMV viral load  
E. Blood for quantitative JC viral load

Correct answer: C

Rationale:

The principal concern in this patient is possible BK virus nephropathy. Although quantitative PCR of plasma or urine has been advocated for diagnosis, the most reliable diagnostic measure is demonstration of the characteristic basophilic inclusions in renal tubular cells on renal biopsy. Seeing these tubular cells in urine cytology, “decoy cells” is too common to be diagnostic, though absence of these cells suggests against the diagnosis. BK, a polyoma virus, cannot be cultured by routine measures and large quantities can be found by PCR of urine from immunosuppressed patients without nephropathy. JC virus causes progressive multifocal leukoencephalopathy, not nephropathy. Neither CMV nor EBV cause renal failure.
Question # 36

A 63-year-old man with HIV infection has received many different antiretroviral agents, with poor response to each related to poor adherence.

His current genotype, on his current drugs, shows the following:

- RT: M41L, L210W, T215Y, Y181C, Y188C
- Pro: I47A, I50L, V82A, L90M

Which is the most correct regarding his potential response to raltegravir?

A. Raltegravir resistance is linked to these protease genotypes.
B. Raltegravir resistance is linked to these reverse transcriptase genotypes
C. If this patient fails a regimen containing raltegravir, the emerging virus is not likely to be raltegravir resistant.
D. If this patient fails a regimen containing raltegravir, there are likely to be two or more raltegravir resistance mutations.

Correct answer: D

Rationale:

D is correct; there are two paths to raltegravir resistance (Q148 and N155), but both usually (but not always) require two or more mutations for clinically important resistance to occur.

Resistance mutations involving RTIs, NNRTIs or PIs do not predict raltegravir resistance, so that A and B are wrong.

When patients fail raltegravir containing regimens, they often have raltegravir resistance occurring via one of the two pathways mentioned above.