SESSION 4 | TUESDAY, AUGUST 24, 2021

Session Moderator: Dr. Gulick
Session Panelists: Drs. Bloch, Dorman, Dupont, Maldarelli, Saag, and Weinstein

46 | NOROVIRUS | DUPONT

An 88-year-old man who lives in a nursing home in a large U.S. city develops diarrhea and vomiting. He has not recently taken antibiotics and is not on a proton pump inhibitor. He develops diarrhea and is taken to a hospital where he is found to have advanced renal failure and ventricular arrhythmia and despite fluid therapy and cardiovascular drugs he dies 12 hours after admission.

Which of the following is the most likely cause of his enteric syndrome and death?

A. Norovirus
B. *Aeromonas*
C. *Listeria monocytogenes*
D. *Shigella*
E. *Campylobacter*

Correct answer: Norovirus

Norovirus infection is the second most important cause or death associated with diarrhea in the U.S. (~800 deaths per year). These deaths are almost all in elderly people in nursing homes. Losing fluid and salt from both ends of the GI tract in elderly patients sets them up for renal failure and electrolyte depletion with arrhythmias.

The pathogen causing more deaths is *C. difficile*, which would be a good guess, but no more likely than norovirus in an elderly person in a nursing home with vomiting and not taking antibiotics or PPIs.

Aeromonas is a diarrhea pathogen in diarrhea especially in people living in tropical regions. It can cause bloody and persistent diarrhea. It is not common in the U.S. and isn't an upper GI tract disease with vomiting.

Listeria monocytogenes causes short lasting febrile diarrhea seen occasionally in foodborne outbreaks and shows a low mortality rate, in contrast to bacteremic or central nervous system infection by the organism, which is without vomiting and diarrhea.

Shigella and *Campylobacter* would be exceedingly rare in someone confined to a nursing home and would produce more dysentery than vomiting and would not be rapidly fatal.

47 | TRAVELER'S DIARRHEA RX | DUPONT

A 40-year-old healthy traveler to Nepal develops diarrhea consisting of passage of 2 soft stools/d with mild cramps. This has persisted for 9 days. She is able to do what she came to do but needs to know where bathrooms are located at all times.

What would you recommend she do about her enteric syndrome?

A. Ciprofloxacin 500 mg bid for 3 days
B. Azithromycin 1,000 mg single dose
C. Rifaximin 200 mg tid for 3 days
D. Fluids (soups, broth, non-carbonated drinks) only with or without loperamide she has with her
E. No therapy

Correct answer: Fluids (soups, broth, non-carbonated drinks) only with or without loperamide she has with her

Previous recommendations were to treat all patients with traveler's diarrhea with antibiotics because more than 80% of diarrhea of travelers to developing regions is caused by a bacterial pathogen. Travel medicine experts now advise that antibiotics be used only in travelers with more severe and disabling diarrhea. The concern is encouragement of colonization of ESBL-resistant Enterobacteriaceae while in a setting of low hygiene, where these organisms are so prevalent.

Some studies in Southern Asia where she is going have shown that more than half of patients with travelers' diarrhea taking antibiotics will be colonized by ESBL-resistant *Escherichia coli* that may persist for up to a year and spread to family members on returning home complicating treatment of UTIs or post-operative infections.

Rifaximin has not been studied for resistance acquisition but may be safer than the other antibiotics.

Another licensed rifamycin, Rifamycin SV-MMX, licensed in the U.S. and Europe for travelers' diarrhea has been shown in two studies to not increase colonization of resistant bacteria.

The best answer, especially for an examination question is electrolyte-containing fluids and symptomatic treatment. Loperamide can control stooling and is not a concern for disease potentiation in non-dysenteric, afebrile patients with diarrhea.

48 | 2-Drug Combo HIV | Gulick

A 44-year-old man recently diagnosed with HIV is concerned about drug side effects and wants to start an ART regimen with the "lowest number of drugs possible."

Which of the following initial regimens is optimal for his initial therapy?

A. bictegravir monotherapy
B. boosted darunavir + lamivudine
C. dolutegravir/lamivudine
D. dolutegravir/rilpivirine

Correct Answer: dolutegravir/lamivudine

The GEMINI study demonstrated that an initial 2-drug combination regimen of dolutegravir/lamivudine was non-inferior to a standard 3-drug regimen of tenofovir disoproxil fumarate (TDF) /emtricitabine/ dolutegravir and this is now listed among first-line ART options in current guidelines.

No monotherapy regimen is recommended for initial (or maintenance) therapy.

A boosted protease inhibitor + lamivudine demonstrates significant virologic activity as either initial or maintenance therapy, but is a 3-pill/3-drug regimen.

The single-pill dolutegravir/rilpivirine is a one-pill regimen indicated for maintenance therapy in patients with virologic suppression on other ART regime. This drug has not been tested or approved as initial therapy.

Dolutegravir/rilpivirine is indicated as a complete regimen for the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed on a stable antiretroviral regimen for at least 6 months with no history of treatment failure and no known resistance mutations.

49 | TB Peritonitis | Dorman

A 36-year-old female is referred to ID clinic from the Gynecology Department, where she had presented with 6 months of abdominal discomfort and swelling, accompanied by 12 lb weight loss and fevers. She was originally from Brazil and had moved to the US four months prior. She has severe, poorly controlled asthma and has received several steroid tapers over the past year. Evaluation by the Gynecology team had included CA-125, which was elevated at 608 U/ml (normal range <35 U/ml). CT imaging of the abdomen and pelvis showed ascites and omental caking.

Laparoscopy was performed and on visual inspection there was diffuse studding of intraperitoneal surfaces with 2-3 mm tan nodules. A biopsy of affected material was obtained and showed non-caseating granulomas without evidence of malignancy; cultures were set up and are in progress.

What is the most likely mode of transmission of the infection?

A. Bite of a triatomine (kissing bug) insect
B. Bite of a sand fly
C. Inhalation of airborne bacteria
D. Sexual transmission of a spirochete

Correct answer: Inhalation of airborne bacteria

Her presentation is compatible with abdominal tuberculosis caused by *Mycobacterium tuberculosis*, and she has an epidemiological risk (prior residence in Brazil). TB peritonitis can cause elevated levels of CA-125 and present as a clinical mimic of ovarian carcinoma with peritoneal carcinomatosis. While caseating granulomas are commonly seen in tuberculosis, non-caseating granulomas can also occur in tuberculosis, particularly in immunocompromised individuals.

Residence in Brazil puts her at some risk for Chagas disease caused by *Trypanosoma cruzi*, which is transmitted through the bite of triatomine insects, as well as leishmaniasis (transmitted through bite of a sand fly), but her presentation is not compatible with these infectious diseases. Syphilis is caused by sexual transmission of the spirochete *Treponema pallidum*, but this patient's clinical presentation is not compatible with either early or late syphilis.

50 | LATENT TB | DORMAN

An 18-year-old male is referred to you for evaluation and management of a positive QuantiFERON-TB Gold test. He was born in India and is in the U.S. as a high school exchange student. He reports no significant past medical history, and he feels entirely well without cough, fevers, or weight loss. To his knowledge he has never been in contact with anyone with pulmonary TB. Records from the referring provider document a negative HIV test, normal CBC and liver chemistries, and a normal chest X-ray, all performed 2 weeks ago.

What is the best next step?

A. Recommend treatment for latent TB infection with 2 months of rifampin and pyrazinamide
B. Recommend treatment for latent TB infection with 12 weeks of once weekly isoniazid and rifapentine
C. Perform a tuberculin skin test to make sure that this is not a false-positive QuantiFERON-TB Gold test
D. Initiate TB treatment with rifampin, isoniazid, pyrazinamide, ethambutol

E. No further action needed since the positive QuantiFERON-TB Gold test most likely represents immunological cross-reactivity to neonatal vaccination with Bacille Calmette-Guerin (BCG)

Correct Answer: Recommend treatment for latent TB infection with 12 weeks of once weekly isoniazid and rifapentine

The clinical picture is one of latent TB infection, making (d) incorrect. (a) is incorrect since a regimen of 2 months of rifampin plus pyrazinamide is no longer a recommended treatment regimen for latent TB infection due to high rates of hepatotoxicity.

BCG vaccination can cause a positive tuberculin skin test due to cross-reaction antigens between BCG vaccine and purified protein derivative. However, the QuantiFERON-TB Gold test includes only stimulatory antigens that are absent from BCG and thus prior BCG vaccination does not cause a positive QuantiFERON-TB Gold test (this is the major advantage of QuantiFERON-TB Gold in individuals who have received prior BCG vaccination). For this reason, (c) and (e) are incorrect.

51 | IBALIZUMAB | SAAG

A 71 y/o man with HIV disease transfers care to you with a history of taking and failing "nearly all HIV medications including T20 (enfuvirtide)".

He currently takes tenofovir alafenamide (TAF)/emtricitabine (FTC) + etravirine + darunavir + ritonavir with a CD4 15 and HIV RNA 233,140 copies/ml.

You send an HIV genotype, phenotype, and tropism test. The tropism test returns "dual/mixed virus".

In addition to optimizing his antiretroviral regimen, you recommend:

A. Adding maraviroc
B. Adding double-dose maraviroc
C. Adding enfuvirtide
D. Adding ibalizumab

Correct answer: Adding ibalizumab

This patient has advanced multidrug resistant HIV disease and needs every opportunity to suppress his viral load and increase his CD4 cell count.

In addition to optimizing other classes, the HIV entry inhibitors could provide virologic activity. However, he's taken T-20 (enfuvirtide) and is highly likely to be resistant and having dual/mixed virus means that maraviroc (at any dose) does not have significant activity.

This leaves two more recently approved HIV entry inhibitors (a post-attachment CD4 receptor inhibitor, ibalizumab, and a CD4 attachment inhibitor, fostemsavir), each with its novel mechanism of action that should retain full virologic activity. Optimally, ibalizumab or fostemsavir are combined with other active antiretroviral drugs in the subsequent regimen.

52 | HLA ABACAVIR | SAAG

A 22 y/o man is found HIV+ with a CD4 344 and HIV RNA 16,000 copies/ml and starts abacavir (ABC)/lamivudine (3TC)/dolutegravir(DTG) at an outside clinic.

After several days, he develops a rash, nausea and vomiting for which he does not seek medical attention. He discontinues his medications and feels much better.

Three months later, after urging from his mother, he presents to you now to restart HIV therapy.

He is asymptomatic, has a normal physical exam, CD4 322, and HIV RNA 15,000 copies/ml.

What do you advise regarding ART?

A. Repeat CD4 and HIV RNA
B. Check G6PD before restarting ART
C. Check HLA-B*5701 before restarting ART
D. Restart ABC/3TC/DTG with instructions to call clinic for any symptoms

Correct answer: Check HLA-B*5701 before restarting ART

There is no record of this patient having had HLA-B*5701 testing before being prescribed abacavir (ABC) and he presents with a history that could be consistent with an ABC-hypersensitivity reaction.

If this was ABC hypersensitivity, rechallenge with ABC could lead to hypotension or even death. He should have HLA-B*5701 tested and if negative, ABC/3TC/DTG could be resumed; alternatively he could be switched from ABC/3TC to tenofovir (AF or DF)/FTC.

53 | KPC OUTBREAK | WEINSTEIN

Over a 3-week period, 5 patients in a 12-bed ICU have infections with a carbapenem-resistant *Klebsiella pneumoniae* (KPC): Two have symptomatic urinary tract infections, 2 have ventilator-associated pneumonia, and 1 has a line-related bacteremia. These are the only KPC infections recognized in this ICU in the past 6 months.

Whole genome sequence (WGS) analysis of the isolates shows that four are nearly identical and one probably genetically unrelated.

The most likely epidemiologic explanation for these infections is that this cluster represents which of the following:

A. Is a pseudoepidemic
B. Results from lapses in infection control
C. Results from common source medication contamination
D. Represents a water-borne outbreak
E. Represents a food-borne outbreak

Correct answer: Results from lapses in infection control

Pseudoepidemics usually reflect surveillance, diagnostic, or lab errors — unlikely in this scenario. So, the occurrence of a cluster of KPC likely is a real epidemic. The occurrence of a predominant WGS-type and the multiple different sites of infection suggest cross-infection due to poor infection control practices. The other explanations – water, food, or medication contamination — would not explain the sites of infection and are unlikely based on the known current epidemiologic behavior of KPC. The existence of 2 WGS types suggests 2 separate introductions of KPC into the ICU.

54 | EPIGLOTTITIS | BLOCH

A 56-year-old female presents c/o sore throat. She was in her usual state of health until 1 day prior to admission when she noted pain on swallowing and myalgias. A rapid strep test at a walk-in clinic was negative and she was given a presumptive diagnosis of viral pharyngitis. That evening the pain progressed and she presented for ER evaluation.

She lives in rural Idaho and has well water. She raises chickens and has a pet goat. She has not travelled outside of the region in the last year. She notes exposure to her 2-year-old grandson who had a fever the previous week.

On presentation she is afebrile and vitals signs are stable. She is breathing comfortably on room air without stridor however she is spitting into a cup next to the bed because it hurts to swallow. Oropharyngeal exam shows good dentition, normal mucosa and no tonsillar enlargement or inflammation. There is no cervical swelling or lymphadenopathy.

White blood cell count is 15.9, other labs are unremarkable.

Which of the following is the most likely diagnosis in this patient?

A. Ludwig's angina
B. Streptococcal pharyngitis

C. Diphtheria
D. Pharyngeal tularemia
E. Epiglottitis

Correct answer: Epiglottitis

In contrast to children, epiglottitis in adults presents sub-acutely. Classic findings in pediatric patients such as muffled speech (the classic "hot potato" voice), stridor and tripod posturing are rarely present in adults, in whom sore throat and odynophagia are the most common symptoms. This may relate to differences in microbiology: The classic organism in children is *Haemophilus influenzae*, whereas in adults, other organisms, particularly *S pneumoniae,* predominant. Another key difference is the low risk of acute airway closure precipitated by exam, and laryngoscopy in adults is typically both safe and diagnostic. When epiglottis is suspected, regardless of patient age, the most immediate concern is securing the airway, with initiation of broad empiric antibiotics (in adults, vancomycin plus a 3rd generation cephalosporin) a secondary priority.

Epiglottis can be differentiated from the other choices by the physical exam.

Ludwig's angina is infection of the submandibular space, and typically follows an odontogenic infection. Patient's present acutely ill, with pain and swelling in the floor of the mouth. The classic physical exam finding, woody submandibular induration, was absent in this patient.

Streptococcal pharyngitis may present similarly to epiglottis, with sore throat and fever. The negative rapid antigen diagnostic test is only about 80% sensitive, so this would not definitively exclude the diagnosis. However, on physical exam, patients with streptococcal infections have enlarged and inflamed tonsils with purulent exudate, which was absent in this patient.

Diphtheria can cause a sore throat and odynophagia. The clue on the physical exam is the presence of a gray coating adherent to the posterior pharynx. Diphtheria is an important cause of pharyngeal infection internationally but would not be a concern in the absence of travel, reflecting the effectiveness of vaccination in the US.

Tularemia can rarely involve the pharynx, usually after ingestion of contaminated water or food. This patient's history of well-water ingestion might be compatible with this. However, patients with pharyngeal tularemia are typically quite toxic, with exudative pharyngitis and suppurative lymphadenopathy, which were not present in this case.

55 | BABESIA | BLOCH

A previously healthy 29yo female presents with 1 week of fevers, chills, and headache. She decided to seek medical care after she noted dark discoloration of her urine.

She lives in Connecticut and has a vacation home on Martha's Vineyard. She is an avid hiker and notes many tick and mosquito bites in the last month. She has traveled extensively for work, including a trip to South Africa 1 year previously where she visited a game preserve.

On physical exam, her temperature is 102.8 F, heart rate is 118 bpm, and BP is 125/68. Otherwise, exam is unremarkable, with no rash, photophobia, or nuchal rigidity.

Laboratory studies include:

- WBC=5.8
- H/H=7.4/22
- Platelets=97

- AST/ALT=127/119
- Alk phos=384
- Total Bilirubin=1.7

- Haptoglobin <8
- LDH 784

- A lumbar puncture was done, with 1 WBC

A Giemsa stain of a thin blood smear is below:

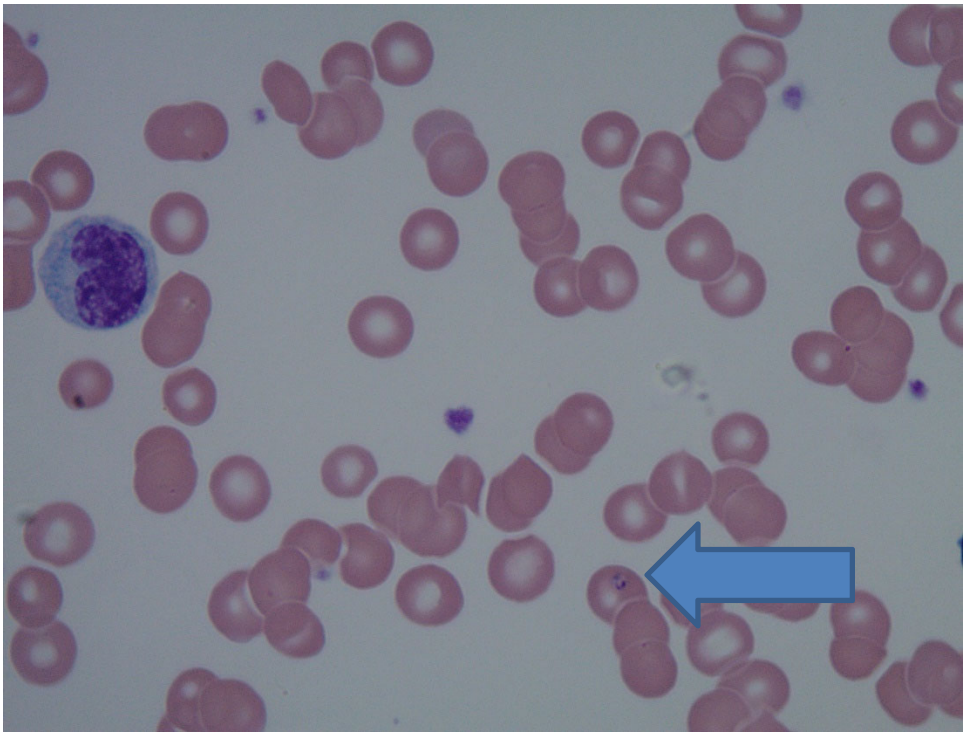

Photo courtesy of Alex Maris, MD PhD

Which of the following pathogens is the most likely cause of her illness?

A. Plasmodium falciparum
B. Powassan virus
C. Babesia microti
D. *Anaplasma phagocytophilum*
E. *Plasmodium knowlesi*

Correct answer: Babesia microti

Babesiosis is an infection caused by an intra-erythrocytic protozoan parasite, most commonly *Babesia microti*. The *Ixodes scapularis* tick, which is endemic to the Northeast, Mid-Atlantic, and upper Midwest, is the vector for this infection. Symptoms are nonspecific and include fever, headache, and myalgias. Because this organism is trophic for red blood cells, hemolysis is frequently present, and signs and symptoms related to this include bilirubinuria, jaundice, scleral icterus, hepatomegaly, and splenomegaly (and rarely, splenic rupture). Severe disease is more common in older, immunosuppressed, or asplenic patients, and correlates with the degree of parasitemia.

Laboratory findings suggestive of babesiosis are related to the presence of hemolysis. Anemia, elevated liver function tests, and markers of hemolysis (low haptoglobin, elevated LDH, elevated reticulocyte index) are clues to this diagnosis. Confusion may be present due to encephalopathy, but

CNS involvement is not a feature of babesiosis, and CSF evaluation is only indicated if needed to exclude other pathogens.

A provisional diagnosis can be made based on visualization of protozoa in red blood cells. The trophozoites are often ring shaped and may mimic *P. falciparum* microscopically. A pathognomonic finding of babesiosis is the presence of a tetrad or Maltese Cross inside red blood cells. In contrast to *P falciparum*, banana-shaped gametocytes are not seen. Microscopy is less sensitive than PCR for the diagnosis of babesiosis.

Geography is an important consideration in differentiating babesiosis from malaria due to *P falciparum.* This case was complicated by the history of travel however *P falciparum* malaria typically occurs within one month of exposure and therefore distant travel is unlikely to be relevant. *P. knowlesi* is endemic in Southeast Asia, not Africa, and malaria due to this organism presents acutely as well.

Powassan virus and *A. phagocytophilum* are also spread by *Ixodes* ticks and therefore endemic to the same regions as *Babesia microti*. Powassan virus causes meningoencephalitis and does not persist intra-cellularly. Hemolysis is not associated with Powassan virus infection and a blood smear would not be helpful in making the diagnosis.

A. phagocytophilum causes human granulocytic anaplasmosis (HGA), which typically presents as a nonspecific febrile illness. This organism is tropic for neutrophils, and buffy coat examination reveals cytoplasmic inclusions in PMNs in >50% of patients. Erythrocytes are not infected, and hemolysis is not a feature of HGA.

56 | PrEP | Gulick

A 28 y/o HIV negative woman with an HIV+ male sexual partner asks about taking HIV pre-exposure prophylaxis (PrEP).

Which do you recommend?

A. None, PrEP not indicated
B. Daily tenofovir disoproxil fumarate (TDF)/emtricitabine
C. Episodic TDF/emtricitabine
D. Daily tenofovir alafenamide (TAF)/emtricitabine
E. Episodic TAF/emtricitabine

Correct answer: Daily tenofovir disoproxil fumarate (TDF)/emtricitabine

HIV PrEP reduced the risk of acquiring HIV in both men and women, with some important differences among the tested regimens.

While studies demonstrated daily TDF/emtricitabine works for both men and women, daily TAF/emtricitabine ONLY was studied in men and episodic TAF/emtricitabine has not been studied at all.

Newer injectable PrEP regimens (e.g., cabotegravir/rilpivarine) for both men and women show promise in clinical trials, but are not yet FDA approved for PrEP, although this injectable is approved for therapy in patients who have been virologically suppress on a stable regimen with no history of treatment failure and no know resistance to either cabotegravir or rilpivarine.

57 | GENOTYPING | MALDARELLI

26-year-old HIV+ man on his first ART regimen, tenofovir (TDF)/emtricitabine + raltegravir, for 2 years. HIV RNA originally 203,000 copies/ml, then decreased to <50 copies/ml by 4 months.

On his most recent routine lab tests, HIV RNA was 13,900 copies/ml, repeated 2 weeks later after adherence counseling at 11,400 copies/ml.

What lab test(s) would you now order?

A. Drug level testing
B. Genotype testing (reverse transcriptase/protease and integrase)
C. Phenotype testing (reverse transcriptase/protease and integrase)
D. Genotype and phenotype testing (reverse transcriptase/protease and integrase)
E. CCR5 tropism testing

Correct Answer: Genotype testing (reverse transcriptase/protease and integrase)

This patient is experiencing virologic failure (likely due to adherence issues) on a nucleoside reverse transcriptase inhibitor- and integrase inhibitor-containing regimen and should have drug resistance testing done. For first regimen failure, genotypic testing (alone) is the recommended test.

For multiregimen failure, both genotypic testing (reverse transcriptase/protease and integrase) AND phenotypic testing (reverse transcriptase/protease) is recommended. Drug level testing and phenotypic testing of integrase inhibitors are not routinely recommended.

CCR5 tropism testing is only recommended if maraviroc is being considered as a treatment option.

58 | PEP | MALDARELLI

A 23 y/o man presents to the emergency room asking for "HIV PEP" (post-exposure prophylaxis).

He states that he had receptive anal intercourse 2 hours ago with a male partner with unknown HIV status and that "the condom broke."

He is in good health and a rapid HIV antigen/antibody test is negative.

What do you recommend?

A. No PEP – low-risk exposure
B. Start PEP when HIV drug-resistance testing results available
C. Start PEP now with zidovudine/lamivudine + lopinavir/ritonavir
D. Start PEP now with tenofovir (TDF)/lamivudine + dolutegravir
E. Start PEP now with single-dose nevirapine

Correct Answer: Start PEP now with tenofovir (TDF)/lamivudine + dolutegravir

While the HIV status of the source is unknown, this is a high-risk exposure and PEP would be reasonable to recommend. PEP should be started immediately and among the suggested regimens, current guidelines recommend tenofovir (TDF)/lamivudine + dolutegravir (or raltegravir) for potency, tolerability, and convenience.

The older PEP regimen, zidovudine/lamivudine + lopinavir/ritonavir, causes significant gastrointestinal side effects and should be avoided.

Single-dose nevirapine was used previously to prevent mother-to-child transmission, but is NOT well-tolerated in HIV-negative individuals and given as a single drug, commonly leads to HIV drug resistance, and consequently is not recommended for PEP use.

59 | HCV | SAAG

A 32-year-old man returns for routine follow up in the HIV clinic and is found to have new elevations in his liver function tests.

He has no complaints and his physical exam is normal.

Lab evaluation from this visit reveals:

- Normal electrolytes
  - AST 130 u/ml (35 u/ml last visit)
  - ALT 180 u/ml. (25 u/ml last visit)
  - Bilirubin 0.8 mg/dl

- Alk phos 110 mg/dl

- RPR non-reactive
- Urine / rectal NATs negative for GC and Chlamydia

He has been on BIC / FTC / TAF (Biktarvy-bictegravir, emtricitabine & tenofovir alafenamide) for the last 2 years with undetectable virus. His last CD4 count 1 year ago was 855 cells /ul.

Three years ago he was diagnosed with HCV (no evidence of cirrhosis on fibroscan at that time) and he received treatment with sofosbuvir and ledipasvir for 12 weeks, achieving an undetectable HCV RNA at month 4 post-treatment.

At the time of his HCV treatment he was vaccinated for Hepatitis A and Hepatitis B. His post vaccine hepatitis B surface antibody (anti-HBs) titer was >10 milli-international units/mL.

He reports frequent sexual activity with same sex partners; at least 4 – 6 different partners per month over the last 5 months.

Which of the following is most likely responsible for his increased liver enzymes:

A. Hepatitis A infection
B. Hepatitis B infection
C. Hepatitis C infection
D. Drug induced liver injury (DILI)
E. Cirrhosis

Correct answer: Hepatitis C infection

This patient has been reinfected with HCV.

Hepatitis C is transmitted via intravenous drug use and via sexual activity, especially among MSM. The patient was cured of his hepatitis C infection with sofosbuvir-ledipasvir therapy 3 years ago as evidenced by a sustained virologic response (SVR) 4 months after cessation of therapy, which is tantamount of a cure.

Ongoing exposure to others with untreated HCV likely led to re-infection (answer C), which was manifest as elevated liver enzyme tests, and can occur despite having prior immunity to HCV infection. Any spike in liver enzyme tests in a sexually active MSM, even if previously cured, is an indication for HCV screening with HCV RNA testing.

Of note, HCV antibody tests will be positive for life after his initial HCV infection and is not indicative of reinfection; only a new, detectable HCV RNA value (usually > 1000 c/ml) is diagnostic of new HCV infection.

Hepatitis A and B infections (answers A and B) are highly unlikely owing to prior vaccination. It is true that his antibody to HBV may have waned since it was last tested. Unlike HCV, HAV and HBV infection is largely prevented with established immunity, in this case from a vaccine. Moreover, incident HBV infection is unlikely in a patient on tenofovir.

- Remember regarding HBV: A positive immune response to HBV vaccination is defined as the development of hepatitis B surface antibody (anti-HBs) titer >10 milli-international units/mL. However, since most patients respond to vaccination, post-vaccination testing is only indicated in select persons with ongoing risk (e.g., health care and public safety workers, **sex partners of HBsAg-positive patients**) and/or those who are less likely to respond to the vaccine (e.g., patients on chronic hemodialysis, **persons with HIV**, patients receiving immunosuppressive therapy).

Drug induced liver injury (DILI; answer D) is manifest with elevation of AST, ALT, and bilirubin (Hy's Law). An elevated bilirubin was not present in this case.

Finally, the patient had a fibroscan 3 years ago that showed little to no evidence of scarring, which along with no clinical features of end-stage liver disease, rules out cirrhosis.

60 | LOW CD4 | GULICK

A 62-year-old man with newly diagnosed HIV infection (HIV RNA 326,000 copies/ml, CD4 205 cells/uL) starts antiretroviral therapy with tenofovir alafenamide (TAF)/emtricitabine/bictegravir. At 3 months, this patient had an HIV RNA is <20 copies/ml and CD4 211 cells/uL.

At 6 months, HIV RNA <20 copies/ml and CD4 203 cells/uL.

He's concerned about his CD4 cell count.

What do you recommend?

A. Continue present ART regimen
B. Change TAF/emtricitabine to ABC/lamivudine
C. Change bictegravir to darunavir/ritonavir
D. Add darunavir/ritonavir
E. Start filgrastim (G-CSF)

Correct Answer: Continue present ART regimen

This patient started on appropriate first-line ART and achieved maximal virologic suppression, but failed to increase his CD4 cell count. This occurs in ~10% of people and is more common with older age or lower baseline CD4 cell count (and in this case, both).

Neither changing nor adding antiretroviral drugs to an already suppressive regimen has been shown to increase CD4 cell counts.

Thus, this regimen should be continued, other potential causes of lymphopenia evaluated, and the patient reassured that they are benefiting from the virologic suppression.