Case Discussions

National HIV Curriculum Podcast

Initial Laboratory Evaluation of a Person with HIV

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National HIV Curriculum Podcast Editors Dr. Jehan Budak and Dr. Aley Kalapila discuss their approach to the initial laboratory evaluation with a person newly diagnosed with HIV, including HIV-specific, co-infection screening, and healthcare maintenance labs.

Topics:

- OIs and HIV
- hepatitis
- STI
- TB

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Transcript

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In this episode:

introduction**[00:00] Introduction**

Hello, everyone. I'm Dr. Jehan Budak from the University of Washington in Seattle, and welcome to the National HIV Curriculum Podcast. This podcast is intended for health care professionals who are interested in learning more about the diagnosis, management, and prevention of HIV.

I'm back with my colleague, Aley Kalapila, an ID physician at Emory University in Atlanta. Hi Aley!

Dr. Kalapila

Hi Jehan. Hi everyone listening, excited to be back here and to do this episode.

Dr. Budak

So, today we're going to pick up where we left off regarding the evaluation of a person who is new to the clinic and establishing care for HIV management and other primary care needs. Whereas in the earlier episode, we talked about establishing rapport and the questions and history we would take. Since that initial visit and evaluation can be complex and an emotional experience, we've not yet discussed the lab workup we would get. And to clarify, today we are discussing tests we would obtain when someone already has *confirmed* HIV infection.

three-buckets-approach**[01:00] Three Buckets Approach**

Dr. Budak

So, Aley, let me start by asking, what is your general approach to the lab workup at an initial visit?

Dr. Kalapila

So, I tend to divide those initial labs into three general buckets. We have the HIV-specific and basic labs. We have a bucket that consists of coinfection labs, and then finally health care maintenance labs.

Dr. Budak

Before we go into specifics regarding each of those buckets, can you expand a little bit more about those three categories?

Dr. Kalapila

Sure. So, the first category is HIV-specific and basic labs, and these include labs that are necessary prior to prescribing antiretroviral therapy (ART), and we are also looking here for any organ dysfunction that could impact your antiretroviral therapy choice. Now, this group of labs also helps stage an individual's HIV infection, which is important to determine if the patient may need prophylactic antibiotics.

The second bucket or category of labs are the ones that focus on screening for common coinfections that people with HIV may have, or at risk for, and the presence of which could impact the timing of antiretroviral therapy initiation for example, the choice of ART, and also prophylactic antibiotics, and/or alert us to the need for immunization. And last, but not the least, is the lab evaluation for routine, primary care, or health care maintenance. And of course, this includes evaluation for other non-AIDS, defining comorbidities, such as cardiovascular disease, for example, which is relevant for all people with HIV.

hiv-specific--basic-labs**[02:27] HIV-Specific & Basic Labs**

Dr. Budak

Okay, so with that kind of general overview, let's get into some of the specifics and if you could please start off with the HIV-specific and basic labs.

Dr. Kalapila

So right away, I want to emphasize that, given the relative safety and tolerability of newer antiretroviral agents, we usually don't wait for results prior to prescribing ART. In fact, the Health and Human Services (or HHS) guidelines emphasize ideally prescribing ART within the same day, or within a week, of meeting someone with newly diagnosed HIV. Now, with that in mind, the labs that I would want to get for this specific bucket include a comprehensive metabolic panel (or a CMP), which includes a chemistry panel and liver enzymes, because we want to look for any baseline renal dysfunction and also look for any liver abnormalities. And, we also want to get a complete blood count (or CBC) with a differential because I want to know of any cytopenias, because both the renal dysfunction, liver dysfunction, cytopenias—all of this could have implications on the medications that I might have to prescribe. A common example that we may frequently encounter in practice would be the impact of renal function, for instance, on the ability to prescribe tenofovir-containing regimens.

Dr. Budak

Totally agree. I think that's what I see most frequently. And, another scenario we might encounter might be the presence of cytopenias noted on that CBC, which can then clue us into other coinfections the person may have, whether that be a disseminated infection or an AIDS-associated malignancy.

Dr. Kalapila

That's right. So, in addition to the CBC and the CMP, the other more obvious HIV-specific labs that fall into this category are the CD4 cell count and the HIV RNA (or what we refer to as the HIV viral load). And, this is what allows us to stage someone's HIV infection.

Dr. Budak

And I'd like to clarify that the HIV viral load testing that you're referring to pertains to HIV-1 and not HIV-2. And, as a quick reminder for the listeners, HIV-2 is a strain of HIV not frequently seen in the U.S. but primarily seen in individuals from certain parts of the world, especially in West African countries. Testing for HIV-2 viral loads can only be done at certain labs, and so we recommend consulting with an expert if your patient has HIV-2.

Dr. Kalapila

Agree. And, another point I teach about is that it is important to obtain the HIV RNA and not an HIV DNA, in case that's an option that appears on your order set. As we know, HIV is an RNA virus and so the HIV RNA viral load measures the level of actively replicating virus. Now, this is totally different from the HIV DNA, or proviral DNA, which is the inactive form of HIV that has been integrated into the host cell's DNA and is not helpful in this setting, so always remember you want an HIV RNA viral load.

Dr. Budak

Totally agree! Anything else in this HIV-pertinent lab bucket?

Dr. Kalapila

Yes. So, part of the baseline testing recommendations for all people with HIV is an HIV drug resistance genotype.

Dr. Budak

So, let me talk a little bit about the genotype. The HIV genotype test that we order analyzes the genetic material (specifically that viral RNA that you were talking about, Aley) of the virus in a person's body and is used to identify mutations in the HIV that are associated with drug resistance. The results are compared with known sequences of HIV to check for mutations in genes, such as genes for the reverse transcriptase enzyme or for protease enzyme. And as we know, mutations in these genes can then cause the virus to become resistant to specific drugs, which can then affect the ability to achieve viral suppression.

Dr. Kalapila

Now, Jehan, you mentioned the reverse transcriptase and protease enzymes, but you didn't yet mention checking for integrase resistance mutations. As we both know, the HHS ART guidelines recommend the first-line ART regimens for patients who are treatment naïve contain an integrase strand inhibitor (or INSTI) class of drugs. An example would be the combination of bictegravir with tenofovir and emtricitabine. Yet, the guidelines don't really recommend baseline integrase resistance testing as part of the genotype for people with HIV who are treatment naïve. Why is that?

Dr. Budak

The guidelines recommend standard drug-resistance testing for mutations in the RT (or reverse transcriptase enzyme) and protease genes. And the main reason for the limited use of integrase resistance testing at baseline is that the background prevalence of integrase mutations in treatment-naïve individuals is very low. So, most people starting on INSTIs should respond well, since the mutations that confer resistance to this class, we hope, are rare in untreated individuals.

Dr. Kalapila

That is exactly right. So, this is the reason why HHS guidelines don't recommend routine baseline integrase resistance testing for treatment-naive individuals, unless there is a specific concern for INSTI resistance or other complicating factors. So, examples of such complicating factors could be a patient newly diagnosed with HIV who previously received long-acting injectable cabotegravir for HIV prevention, or a person who has received an INSTI as part of an HIV postexposure prophylaxis (or PEP regimen), or if you're concerned that your patient may have acquired a drug-resistant strain of HIV.

Dr. Budak

Ok, let's move on from the genotype. How about the HLA-B*5701?

Dr. Kalapila

Yes, so, you know that used to be important when we had abacavir as part of our first-line ART regimens, but the HLA-B*57 test is really far less relevant now and it's not something that we typically order, mostly because abacavir-containing regimens are no longer considered first-line treatment for use in ART-naïve individuals. Now, if a provider is, for whatever reason, considering starting a regimen containing abacavir, then you must absolutely check the HLA-B*57 prior to prescribing that abacavir-containing regimen.

Dr. Budak

And that is so that we can avoid an abacavir-associated hypersensitivity, which is a potentially life-threatening allergic reaction to abacavir, characterized by an immune-mediated response. And people who

carry the HLA-B*5701 allele are at significantly higher risk of developing this reaction, which is when the body's immune system mistakenly attacks its own tissues in response to the presence of the drug, and this reaction tends to occur within the first 6 weeks of starting the medication. All this to say, for many reasons, I'm glad that we're not using this as a first-line regimen anymore.

So, I think that's it for HIV-specific labs. anything else, Aley?

Dr. Kalapila

Nothing else to add.

Dr. Budak

Okay, so then let's segue to coinfection screening.

co-infection-screening**[08:56] Co-infection Screening**

Dr. Budak

So, the coinfection bucket includes screening for common coinfections that persons with HIV may already have or are at risk for developing. And we need to assess for these because the presence of certain coinfections can impact timing of ART initiation, choice of ART because of drug-drug interactions, and/or the need for prophylactic antibiotics. So, Aley, can you take us through your approach here?

Dr. Kalapila

I divide this bucket into two separate groups, actually. So, the first are labs that I would get on all people with HIV regardless of CD4 cell count and then the second includes labs that are specific to individuals with a CD4 less than 200.

Dr. Budak

OK, so if you could please start with the labs for people with HIV regardless of their CD4 count.

Dr. Kalapila

So, the main coinfections that are important to test for in all people with HIV, regardless of CD4, are viral hepatitis serologies, STI (or sexually transmitted infection) screening, and tuberculosis (or TB) screening. So, I will start with hepatitis serologies. Now, all patients with HIV should be tested for hepatitis A, hepatitis B, and hepatitis C as part of their baseline lab evaluation at entry into HIV care. For hep A, we need an IgG antibody test to ascertain if a patient has immunity or not. And if not, they would need to be immunized. With hepatitis B, you should triple screen test, looking for a surface antibody, surface antigen, and a core antibody. And, of course, this information's going to help determine if a patient warrants immunization or if their serologies indicate that they have active or prior hepatitis B infection. Active hep B infection *will* impact your HIV antiretroviral therapy choice because you're going to have to pick an ART regimen that has antiviral activity against both HIV and hepatitis B.

Dr. Budak

OK, and how about hepatitis C?

Dr. Kalapila

So, with hepatitis C, we usually check a hepatitis C antibody, which, if positive, then the lab usually reflexively

tests the hepatitis C RNA viral load. And again, this is very important because you want to know if a patient has hepatitis C, because this is a fantastic opportunity to link your patient to hepatitis C treatment with directly acting antiviral agents, which are well tolerated and curative in more than 95% of people!

Dr. Budak

So, what about STIs?

Dr. Kalapila

You have to test for STIs based on the patient's site of exposure, whether or not they have symptoms. So, typically, this would entail a serum test for syphilis, and gonorrhea, and chlamydia testing from any oral or genital mucosal site of exposure. And similarly, you would need urine *Trichomonas* testing for women.

Dr. Budak

Okay, so that was STIs and you had mentioned TB screening as well.

Dr. Kalapila

Now, all patients should have a symptom screen to evaluate for active TB when you're obtaining your review of systems during your initial visit with a patient. But specifically in terms of lab tests, what you're referring to, Jehan, is testing for latent tuberculosis (or LTBI). Now, persons with HIV who have LTBI are at an increased risk of progression to active tuberculosis, and luckily, we have very effective medications to treat LTBI and prevent progression to active TB. So, all this to say, all individuals with HIV should undergo LTBI screening and be offered treatment if they're found to have LTBI (or latent TB). The test that I would use to diagnose LTBI is an interferon gamma release assay, which we often refer to as an IGRA, we abbreviate it as an IGRA. This is a blood test that measures your immune response to the TB bacterial antigens.

Dr. Budak

And I would also add that in some clinical settings, the IGRA may not be available. In which case, the alternative is to do a tuberculin skin test (or a TST) which is when a small amount of protein from the TB bacteria is injected under the skin in the forearm. After 48 to 72 hours, the patient has to return to have the injection site examined by a health care clinician, who measures any induration that may appear at the site. So, since the patient has to return for an evaluation, it's important to coordinate with them and do the TST at a time when they can return to have it read.

Dr. Kalapila

Also, you know, for both the TST and IGRA, another very important teaching point that I like to make is that you should note what the patient's CD4 count was at the time of those tests. If the CD4 is less than 200, then it is important to repeat the LTBI testing once the patient has had immune reconstitution, as both the IGRA and the tuberculin skin test can be falsely negative in an individual with a low CD4 count.

labs-when-cd4-count-below-200**[13:32] Labs When CD4 Count Below 200**

Dr. Budak

Now, let's change gears and talk about tests you order in someone with a CD4 count less than 200?

Dr. Kalapila

Now, this is where I think there may be a lot of practice variability among clinicians. Personally, I see a fair

number of individuals with advanced HIV, so I often tend to obtain these labs on the very first visit, unless I have data ahead of time or a history that is congruent with the patient having a high CD4 count. So, first, I check toxoplasma status with a toxoplasma IgG antibody, because if they have a history of prior toxo infection, then you'd need to ensure your antibiotic prophylaxis choice prevents toxo reactivation. Along these lines, I also tend to get a G6PD level, and this is because the first-line regimen for pneumocystis prophylaxis is trimethoprim-sulfamethoxazole, which we refer to often as trim-sulfa. And, if someone is intolerant of sulfa, for example, then the alternative regimen that's prescribed is dapsone, which should only be prescribed if an individual has normal G6PD levels. So, the G6PD test in my facility often takes a week or more to result, which is the reason why I tend to order it up front.

Dr. Budak

Such a great point. My institution, the CD4 count results either the same day or next day, so I can get add-on additional lab testing as needed. But again, Aley, to your point, I think this is going to be variable depending on, sort of, the context in which you work. Alright, what other coinfection labs do you get?

Dr. Kalapila

So, for patients in whom there's concern for a really low CD4 count, I would get a serum cryptococcal antigen (or a CrAg), because a positive CrAg requires additional workup for cryptococcal meningitis. And, if there's concern or you know that their CD4 count is less than 50, then I would also get a blood culture for acid-fast bacilli (or AFB) because these patients are at risk for disseminated mycobacterium avium complex (or MAC) infection.

Dr. Budak

Okay, so I think that completes the coinfection bucket. Let's move on.

health-care-maintenance**[15:27] Health Care Maintenance**

Dr. Budak

What health care maintenance labs do you order?

Dr. Kalapila

So, we already mentioned getting a CBC and a CMP, which includes a random or fasting glucose, which allows you to screen for diabetes. Now, in addition to that, I would order a lipid panel as part of routine screening for hyperlipidemia. For women of childbearing age, a pregnancy test is of course important because the results would impact regimen selection and need for perinatal monitoring. And last, the HHS recommends baseline urinalysis as part of testing for entry into care to look for the presence of, or risk for, kidney disease.

summary**[16:03] Summary**

Dr. Budak

To wrap up, your three buckets were the HIV-specific and basic labs, which you wanted to get a CBC with differential, a CMP, an HIV RNA, CD4 count, and baseline genotype.

Your next bucket is the coinfection labs, which you subdivided based on CD4 count, and you first started off with saying for all people with HIV, regardless of their CD4 count, that you wanted to test for viral hepatitis serologies, looking for viral hep A, B, and C, and then also get STI screening, as well as screening for latent TB. And then, for the individuals with a low CD4 count, you mentioned getting a toxo IgG, the serum for cryptococcal antigen, and AFB blood cultures.

And last, but not least, is the health care maintenance bucket, where you screened for diabetes, hyperlipidemia, pregnancy, and renal disease. So, I think that's it. Thank you, Aley, for today.

Dr. Kalapila

Thanks, Jehan. See you next time.

credits**[16:58] Credits**

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