Initial Evaluation of the HIV-Infected Adult

In this lecture, we will cover the initial evaluation of the HIV-infected adult. We will focus on how to conduct an initial history and physical examination of a newly diagnosed HIV-infected patient and how to stage the patients' HIV disease severity based on both CDC and WHO HIV classifications.

Case Study

So let us start with a case of a 42-year-old man, a long-distance truck driver, who presented with a 3-month history of painful genital sores.

He tells you that he was diagnosed with HIV several years ago, but never followed up or started treatment since he felt fine up until recently.

Physicians are not magicians! So, you must "Listen to your patient, he is telling you the diagnosis." These are the words of William Osler, the co-founder of John Hopkins University School of Medicine. He helped create the foundation of the discipline of internal medicine and was also instrumental in developing the system of clinical medical education that continues to be used today.[2]

So, the most important question to ask patients is, "How are you feeling?"

We want to know if they are having symptoms or if they feel well.

You have to listen to the patient first and then you can follow up with specific questions, which will enable us to determine the WHO stage.

Patient's History

Let's talk about taking a patient's history.

Specific questions you may wish to ask will include:

- How much weight have you lost?
- Are you able to work?
- Have you ever been hospitalized?
- Are you experiences any fevers? coughing? night sweats?
- Have you ever been diagnosed with TB?
- Are you experiencing any diarrhoea (more than 3 loose BM per day)?
- Do you have headaches, neck pain, weakness in any parts of the body?
- Any genital discharge, itching, ulcers, or other STI symptoms?
- Are you experiences any skin problems or zoster?

Staging

Now let's look at the staging of HIV disease.

There are 2 staging systems: WHO and CDC. Used primarily in low- and middle-income countries, WHO presents 4 clinical stages that are based primarily on clinical signs and symptoms, with a separate immunologic classification system based on CD4 criteria. The CDC staging system, used primarily in high-income countries, includes 3 main stages that rely primarily on immunologic – or CD4 count – criteria, with the exception of CDC stage 3, which integrates a clinical component based on whether any so-called 'AIDS-defining conditions' are present**.**

This is the HIV clinical staging classification system for WHO. As you can see there are 4 stages defined by the presence of a range of clinical conditions that typically occur at different levels of immune dysfunction in PLHIV, with stage 1 being the least severe and stage 4 representing advanced HIV disease.[3]

And this is the WHO immunological classification for HIV. There are 4 stages (none or not significant, mild, advanced, and severe), which are based on slightly different CD4 count criteria depending on the age of the patient.[4]

Before 5 years, the classification uses CD4 *percent*, whereas for adults and children older than 5 years it uses *absolute* CD4 count. Shown here is the current CDC staging system, which was updated most recently in 2014. As you can see, there are 3 main stages that are based primarily on CD4 count criteria.[4]

Stage 1 is the least severe – CD4 count greater than 500.

Stage 2 is when CD4 count is between 200 and 500.

And Stage 3 is the most severe, defined by either a CD4 count less than 200 OR the presence of an AIDS-defining condition.

If an 'AIDS-defining condition is present', the patient falls under CDC Stage 3 no matter what the CD4 count or %. And here is the list of AIDS-defining conditions. If any of these is present, the patient can be classified as having CDC Stage 3 HIV infection, or clinical AIDS. Note that many of the conditions listed here are the same as those used in the WHO clinical staging system as criteria for advanced (WHO Stage 3 or 4) HIV disease.[4]

Return to Case Study

Let's go back to our case.

The patient tells you he has been feeling "not great" for about 3 months, and he occasionally gets fevers. He has taken malaria medicine three times in the past month for fevers at home. He does not know his weight but says that his trousers have been too big for him for several

months and his wife has commented that he appears thin. His appetite is poor and he is often tired.

No history of loose stools but sweats a lot at night.

There is no history of cough.

He drinks alcohol--about 4 bottles in a day. Whenever he is away on a journey he indulges with multiple sexual partners.

Physical Exam

At this point, we should do a physical exam. First, we evaluate the patient's vital signs to determine the need for resuscitation. Is there fever? What are the patient's blood pressure and heart rate? Is the patient in shock? And the respiratory rate—is the patient in respiratory distress? We look at the patient's overall nutritional status by taking anthropometric measures of height and weight to determine the body mass index (BMI). This is calculated by taking the weight in kg and dividing by the height in meters^2.

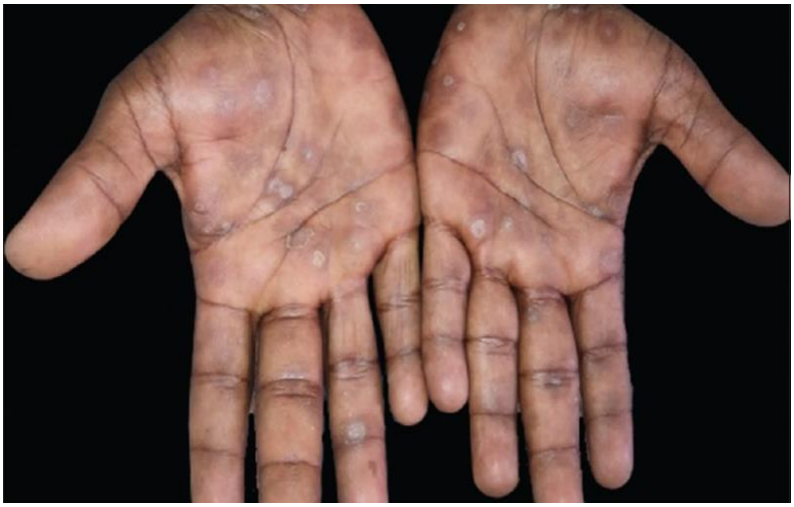
For example, a BMI of less than 18.5kg/m^2 is regarded as underweight.

Next is a general examination with particular attention on lesions that may suggest a background immunosuppression – for example, oral candidiasis (or 'thrush'), as shown here.[5]

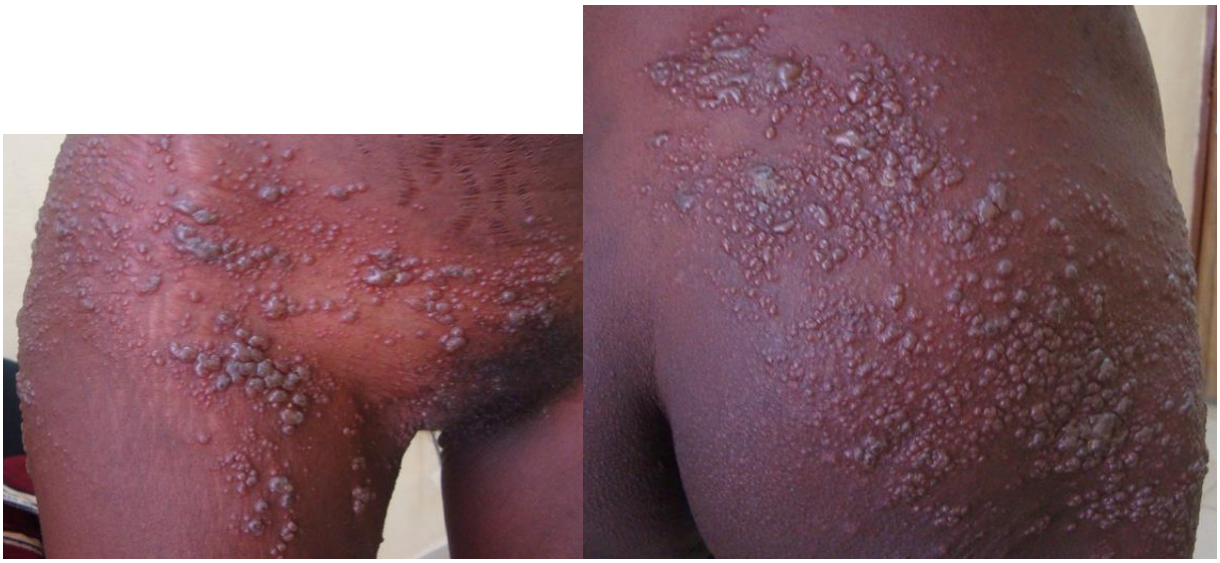
We start from the head and move down to the feet. We look for features of wasting, pallor, dehydration, oral lesion like thrush, apthous ulcers, angular cheilitis, oral hairy leucoplakia, etc. We now look for lymph nodes starting from sub-mental, cervical, supraclavicular, axillary, trochlear lymph nodes etc. Also check the limbs for oedema.

The skin should also be examined for herpes zoster scars/lesions, pruritic popular eruption, Kaposi sarcoma, etc.

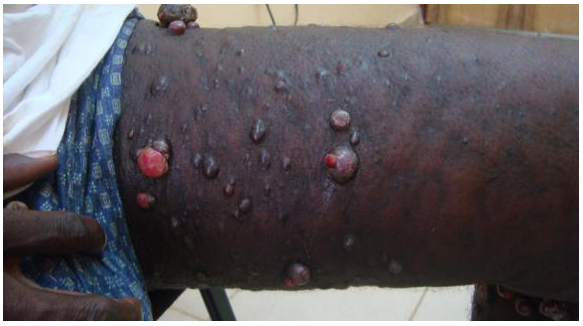
This image shows hyper-pigmented maculo-papular lesions associated with itching, a feature of PPE, which is a WHO stage 2 condition and CDC stage B.[6]



And these photos depict vesicular rashes restricted to L1 and L2 dermatomes on the right side with associated pain are features of Herpes zoaster which is stage 2 WHO and CDC stage B.



Hyper-pigmented macules and nodules with some fungating lesions and associated non-pitting oedema are shown here. These are features of Kaposi's sarcoma, WHO stage 4 and CDC stage B.



Systemic Examination

Finally, perform a thorough systemic examination. In the respiratory system, we look for features of pleural effusion, consolidation, pneumothorax, and so on. For cardiovascular, we look for tachycardia, low BP, distended neck veins, muffled heart sounds, pericardial rub, and so on. In the central nervous system (CNS), we look for meningeal signs, focal neurological deficits, memory deficits, and so on. In the abdominal examination, we check the liver, for an enlarged spleen, tenderness, ascites, and so on.

For women, be sure to palpate the uterus—is it gravid?

Lastly, examine the genitals for genital ulcers, discharge, warts, and so on.

Now we return to our case again!

General examination showed significant wasting of temporalis muscle, prominent zygoma and ribs.

And lymph examination revealed an axillary lymph node that was firm and rubbery, into other significant findings except genital examination which revealed a shallow painful ulcer on the glans penis.

Laboratory Tests

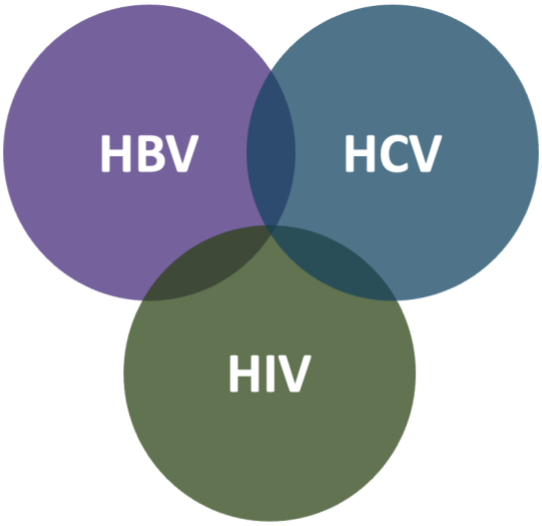
Now we'll discuss which laboratory tests to order. The following tests may need to be ordered:

- A CD4 count, which will help in defining stage of HIV.
- CBC, especially if you're concerned about anaemia or late-stage disease
- Pregnancy test as needed
- RPR, if syphilis suspected and
- Drug resistance testing if possible.

Helpful additional tests in advanced HIV include all of those we just mentioned, plus:

- Cryptococcal antigen
- TB screening: sputum AFB, GeneXpert, chest x-ray
- Liver function test
- Renal function
- Screening for Hepatitis B and C and cervical screening for women.

Other investigations may be required based on your assessment.



HBV, HCV, and HIV infections share common routes of transmission

HBV, HCV and HIV infections share a common route of transmission.

There is an estimated global HBsAg prevalence of 7·4% and a burden of 2.73 million HIV-HBsAg-co-infected persons.

The highest burden for HIV–HBV co-infection is in sub-Saharan Africa with 71% of all cases; and about 1.96 million.

Globally, about 2.3 million persons are co-infected with HIV and HCV viruses, of whom 1.2 million are People who Inject Drugs who are among the key HIV population

HCV-related liver disease has started to overtake AIDS-defining illnesses as a leading cause of death among people living with HIV in some high-income countries. And globally, more people die each year from viral hepatitis than from HIV.

The burden of chronic HBV and HCV remains disproportionately high in low- and middle-income countries (LMICs), particularly in Asia and Africa.

Additionally, even in low-prevalence areas, certain populations have high levels of HCV and HBV infection, such as persons who inject drugs, men who have sex with me, people with HIV, as well as those belonging to certain indigenous communities.

Therefore, PLHIV are an important high-risk group that should be screened for both Hepatitis B and C, and it is very important to test anyone living with HIV for comorbid viral hepatitis at least once.

Tenofovir, which is the major NRTI backbone of HAART is recommended by WHO for treatment of Hepatitis B. Entecavir can also be used.

For Hepatitis C Direct Acting Antivirals are the corner stone for treatment, resulting in cure rates higher than 90%.

Back to Case Study

Returning to our case now, results showed a CD4 count of 184cells/mm^3. Sputum GeneXpert showed no mycobacteria detected but CXR showed extensive streaky and patchy opacities in both lung fields.

Based on the information that you have now, what is the patient's WHO stage?

Does he have early or advanced HIV infection?

The patient has a history of fever, weight loss, and chronic genital ulcers. Investigations revealed a CD4 count of 184 cells/mm^3 and a CXR with features suggestive of PTB.

Therefore, he is at WHO stage 4 and CDC stage C because of PTB, chronic herpes genitals, and a CD4 count of 184 cells/mm^3. Consequently, our patient has advanced HIV infection.

Advanced HIV Disease (AHD)

In general, patients can be classified as early HIV infection (stage 1-2) or **advanced HIV infection** (stage 3-4) based on their WHO stage. WHO defines advanced HIV disease (AHD) as CD4 cell count <200 cells/mm^3 or WHO stage 3 or 4 in adults and adolescents. All children younger than five years of age are considered to have advanced HIV disease. This includes both individuals presenting to care who are antiretroviral therapy (ART) naïve and those returning to care after interrupted treatment.

People with AHD are at high risk of death, even after starting ART; this risk increases with decreasing CD4 cell count.

The most common causes of severe illness and death are tuberculosis, severe bacterial infections, and cryptococcal meningitis.

It should be noted that even patients who are WHO Stage 1-2 and asymptomatic may have low CD4 counts and are still at higher risk of getting sick and dying even when they seem well.

Final Look at Case Study

Let's go back to our case. Does this patient need ART?

Yes, of course.

How urgently should ART be started?

We will discuss the timing of ART initiation in more detail in a different lecture, but in general ART should be started as soon as possible. In patients with low suspicion for TB or cryptococcal disease, WHO recommended immediate ART initiation, even on the same day as diagnosis. However, in this patient, there is a high suspicion for pulmonary TB (based on clinical symptoms of fever, night sweats, weight loss, and CXR findings), therefore ART may be deferred for a period of several weeks. Treatment of PTB takes priority in this case. Management of other co-infections, for example, genital herpes, the likely cause of his painful penile ulcer, should also be undertaken, but should not delay commencement of ART.

However, Septrin prophylaxis must be started immediately, along with the empiric anti-TB therapy.

Summary

In conclusion, be sure to listen to what your patient is telling you so you can learn about their symptoms.

Then you can take a detailed history, which includes their past medical history, what medications they are taking, their family history, and their social history, including their sexual history, substance use history, occupation, and other exposures.

After you perform a physical examination, you will order labs such as a CD4 count so that you can determine the appropriate WHO or CDC stage.

Remember, people with AHD are at high risk of death, even after starting ART and this risk increases with decreasing CD4 cell count.

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