REVIEW

Mini Case for Lab Diagnostics and HIV Review

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Case Description:

A 26-year-old woman presents in your clinic. She has recently immigrated to the US from Uganda. She is sexually active but has not been practicing safe sex. Upon examination, you find vaginal candidiasis. You are highly suspicious of HIV and send a test for ELISA of HIV-1 and HIV-2. These tests come back positive. Confirmation by western blot is received. PCR for HIV RNA and flow cytometry for CD4 are ordered to assess progression of disease.

CD4 Count

CD4 T cells are T-helper cells which are preferentially attacked by HIV infection. One factor in determining the severity of disease, especially risk for infection, is the CD4 T cell count. In order to determine this the clinical laboratory uses fluorescence-activated cell sorting, commonly known as FACS or flow-cytometry to measure the amount of CD4 T cells/μL of blood (Figure 1). This process is represented in Figure 1.

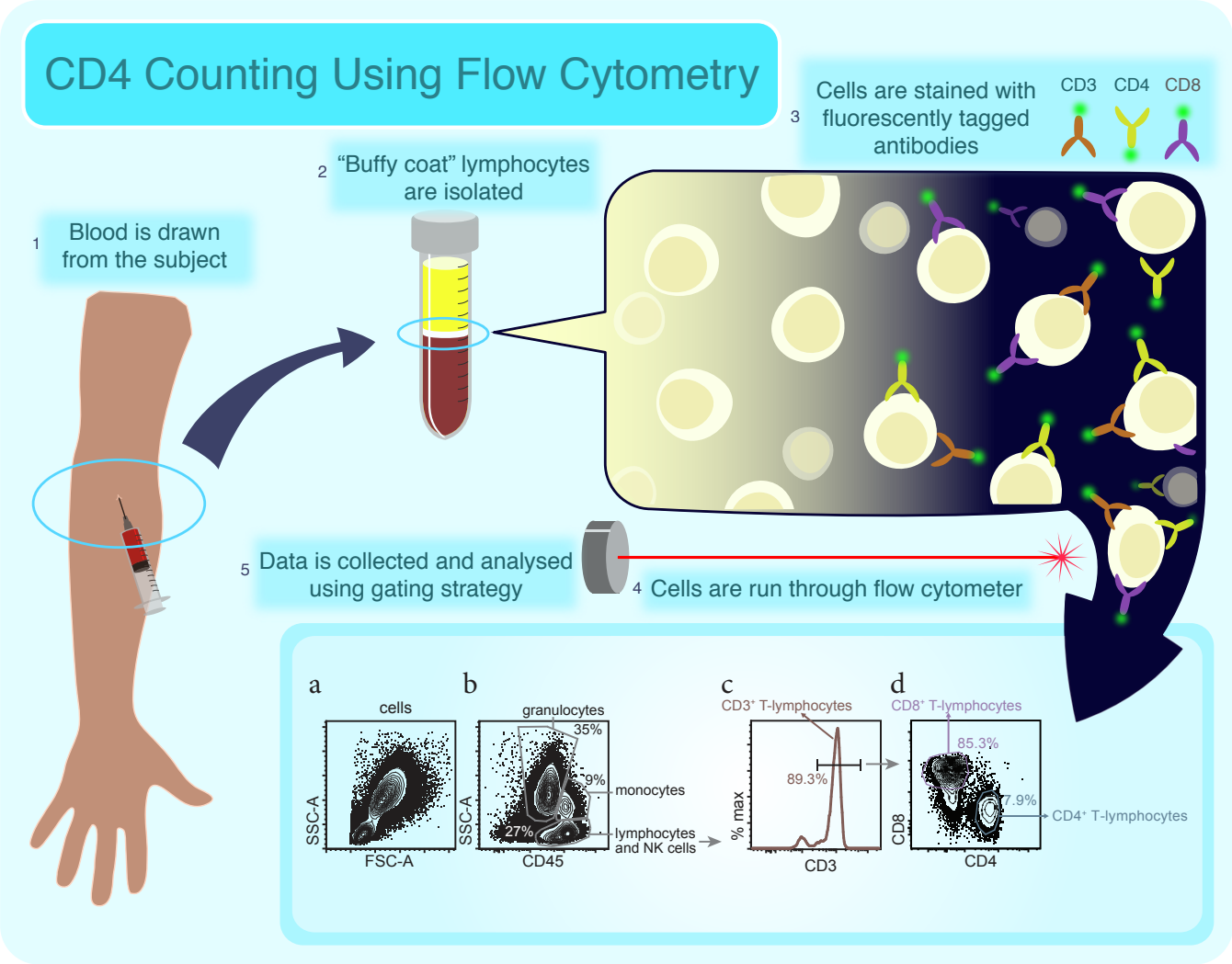

Figure 1. Flow cytometry for CD4 counting. *Image by* **Tziporah Thompson**.

First, white blood cells are isolated from blood by performing a FICOLL, otherwise known as ficoll plaque (Fig 1.2). This process will gradate blood and separate the serum, white blood cells, and RBCs. Next, the cells are stained with antibodies raised against cellular markers that are conjugated to immunoflouresent dyes (Figure 1.3). These antibodies will identify T cells, and more specifically CD4 T cells. Once cells are stained, their fluorescence (and thus, cell type) along with the cell size and granularity are measured by the flow cytometer's laser, producing a diagram of cells which are separable based on size and granularity (Fig1a) as well as by cell markers (Fig1b-c). Once lymphocytes are gated on (Fig1b), CD3 positive lymphocytes are selected (Fig1c). Of CD3 positive cells, we can now identify CD4 and CD8 positive T cells (Fig1d). Here only 7.9% of CD3 positive lymphocytes are also CD4 positive-indicating lymphopenia in this patient.

HIV Progression

We aim here to provide students with an overview of the timeline of HIV infection (Figure 2). Note that not all patients follow this timeline.

ACUTE/EARLY
CD4 ~1000 cells/μL[1]
Presentation: Fever, lymphadenopathy, sore throat, rash, myalgia.

Note on prevention of HIV infection: In order to prevent infection, aside from barrier protection such as condoms, pre-exposure prophylaxis (referred to as "PrEP") was approved in July 2012. PrEP is the pill truvada (a combination therapy containing tenofivir and emtricitabine) and is commonly used to treat HIV. When PrEP is taken consistently by those with risk of getting HIV, is has been shown to reduce risk by up to 92%. See guidelines for providers for more information.[2]

SEROCONVERSION/ VIRAL SET POINT
CD4 ~780 cells/μL[1]
Definition: Development of detectable antibody against HIV, stable viral load.
Presentation: In a study of 7,500 HIV-infected individuals with CD4 counts between 200-499 cells/μL symptoms were[3] : 21.3% thrush (Candida albicans), 9.2% oral hairy leukoplakia, 6.7% herpes zoster, 3.7% paripheral neuropathy.

AIDS
CD4 <200 cells/μL[1] or AIDS-defining illness.
Presentation: Prior to highly-active antiretrovial therapy (HAART): most common presentations (US, 1992-1997)[4]: 36% pneumocystis pneumonia (PCP), 12.4% esophageal candidiasis (Candida albicans), 11.6% Kaposi Sarcoma (HHV-8), 7.8% wasting syndrome, 6.4% Mycobacterium avium.

In the HAART era, AIDS defining opportunistic infections used to be the most common cause of morbidity and mortality. Now, in ART treated patients, non-AIDS mortality has increased compared to opportunistic infections.[5,6]

ADVANCED HIV INFECTION
CD4 <50 cells/μL[1]
Presentation: Varies; most common presentations are cytomegalovirus (CMV) and Mycobacterium avium.

Figure 2. Timeline of HIV infection.

References

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