



CD4 cells in children

their number varies with age



Case study

Victoria age 2, is living with HIV. Her CD4 cell count is $400/\text{mm}^3$ (15%). She is severely growth-retarded and suffers from recurrent oral candidiasis despite appropriate treatment. Her 6-year-old brother, also HIV-infected, has a CD4 count of $380/\text{mm}^3$. He has an itchy skin rash and, like his sister, is being treated with cotrimoxazole.

Victoria's parents don't understand why their daughter must start ART but not her brother, even though he has a lower CD4 cell count.

The role of CD4 cells in the immune system

The immune system protects the body against invasion by foreign bodies such as bacteria, fungi, parasites and viruses. It is made up of organs and antibodies, as well as defence cells found throughout the body: the white blood cells, of which lymphocytes are one type.

CD4 T lymphocytes, which coordinate the immune response, are the main target of HIV. When the virus destroys CD4 cells, the essential functions of the immune system are negatively affected.

The number of CD4 lymphocytes varies with age and with HIV infection

The number of CD4 cells decreases naturally with age

CD4 lymphocytes vary with age and from one person to another, whether infected with HIV or not. A newborn has a very high number of lymphocytes, which decrease naturally. Like all T lymphocytes, CD4 cells are present in high numbers at birth, about $3000/\text{mm}^3$. The number diminishes and stabilises at around the age of 5 years at a level similar to that of an adult, about $800/\text{mm}^3$.

The number of CD4 cells decreases with HIV infection

In individuals living with HIV, the number of CD4 cells decreases over time and with the intensity of viral replication. A high viral load (amount of HIV in the blood) is most often associated with a rapid drop in the CD4 count.

Without antiretroviral treatment, the CD4 count gradually decreases. Below a certain threshold, which varies with the child's age, the body becomes vulnerable to so-called "opportunistic" infections. The AIDS stage corresponds to a critical and life-threatening drop in the CD4 count.

How to interpret the CD4 count in children?

In young HIV-infected children, the number of CD4 cells therefore falls both naturally and because of the HIV infection.

To evaluate the severity of immune deficiency in a child, it is necessary to correlate the child's age with:

- the absolute number of CD4 cells
- or, preferably up to the age of 5 years, the percentage of CD4 cells as compared to the total number of lymphocytes.

One or other of these methods will be used depending on the tests available in the laboratory.

Classification of HIV-associated immunodeficiency in children (WHO 2006)

Immune deficiency	Age - related CD4 values			
	≤11 months	12-35 months	36-59 months	≥5 years
	% (CD4/mm ³)	% (CD4/mm ³)	% (CD4/mm ³)	% (CD4/mm ³)
Not significant	>35%	>30%	>25%	(>500)
Mild	30%-35%	25%-30%	20%-25%	(350-499)
Advanced	25%-30%	20%-25%	15%-20%	(200-349)
Severe	<25% (<1500/mm ³)	<20% (<750/mm ³)	<15% (<350/mm ³)	<15% (<200/mm ³)

CD4 monitoring schedule

In HIV-infected children not receiving antiretroviral treatment, a CD4 count is recommended at least once a year.

For children on ART, a CD4 count should be performed before starting treatment, then every 6 months thereafter (M0, M6, M12, M18, etc.). A CD4 count is recommended before M6 if the clinical response is unsatisfactory.

Changes in the CD4 count are one of the indicators of the immune response to ART. However, before the age of 5 years, a decrease in the CD4 count does not necessarily mean therapeutic failure. It is important to consult the table above to evaluate and interpret any falls in the absolute values or percentages.

Victoria, a child eligible for antiretroviral treatment!

Victoria, 2 years old, is symptomatic with a CD4 count of 400/mm³ (15%). According to the 2006 WHO classification, she has severe immune deficiency,

because her CD4 count is below 20%. She must rapidly be placed on ART.

Her 6-year-old brother, with a CD4 count of 380/mm³, has a mild immunodeficiency, which must be monitored, but ART can probably be postponed for a time. It is therefore more urgent to treat Victoria than her brother.

Key messages

- Up until the age of around 5 years, the absolute number of CD4 cells per mm³ decreases in all children (with or without HIV infection).
- Under the age of 5 years, the CD4 count must be interpreted in relation to the age.
- All infants younger than one year of age with confirmed HIV infection should start antiretroviral therapy, irrespective of clinical or immunological stage; if virological testing is not available a presumptive diagnosis is an ART recommendation. HIV infection must be confirmed as soon as possible.
- A CD4 count should be performed every 6 months for children on ART.

To find out more

- > **The WHO recommendations (2006 revision) for antiretroviral treatment and its indications in HIV-infected children:** Antiretroviral therapy of HIV infection in infants and children in resource-limited settings: towards universal access (2006): immunological assessment of HIV-infected children, **page 17:** <http://www.who.int/hiv/pub/guidelines/art/en/index.html>
- > **The WHO recommendations (2008 revision) for antiretroviral therapy for infants and children:** http://www.who.int/hiv/pub/paediatic/WHO_Paediatic_ART_guideline_rev_mreport_2008.pdf