

Newsletter

HIV INTEGRASE INHIBITORS

Compiled by Dr C Wallis & Dr S Miller

HIV Integrase Inhibitors: Their role in Clinical management

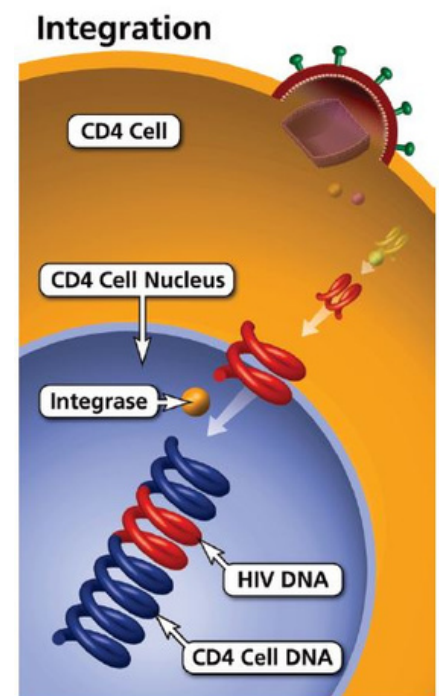
Introduction:

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1. Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs)
2. non-nucleoside/nucleotide reverse transcriptase inhibitors (NNRTIs)
3. Protease inhibitors (PIs)
4. Entry and fusion inhibitors
5. Integrase strand transfer inhibitors (INSTIs)

Integrase strand transfer inhibitors, often abbreviated to "integrase inhibitors", target an enzyme called Integrase, a protein essential for HIV replication. As a result, proviral DNA is unable to insert into the host cell genome. This terminates the life cycle of the virus (see figure on the right).

Three INSTI's have been approved by the FDA: Raltegravir (Isentress), Dolutegravir (Tivicay) and elvitegravir (Vitekta). Raltegravir (RAL) and Dolutegravir (DTG) is registered and available for routine use in South Africa and will be the focus of this clinical update.



Pharmacokinetics

Integrase inhibitors are well absorbed from the upper gastrointestinal tract, and rapidly achieve plasma levels that inhibit viral replication. The antiviral activity of INSTI's is primarily related to trough levels. These are usually well maintained with routine dosing regimens and are largely unaffected by concomitant food ingestion. The HIV-1 viral load declines rapidly using fully active regimens that include an INSTI; a significant proportion of individuals achieve a viral load of < 50 copies/mL within 4 weeks of commencing therapy.

RAL and DTG are primarily metabolized by Glucuronidation in the liver. There is minimal renal elimination; therefore, no dosage adjustment is necessary in patients with renal impairment. Data, however, are lacking on the use of RAL and DTG in individuals on renal dialysis and patients with severe hepatic impairment.

Clinically significant drug interactions

AGENT	RALTEGRAVIR	DOLUTEGRAVIR
Efavirenz	No significant interaction	No significant interaction
Etravirine	No significant interaction	Avoid
Nevirapine	No significant interaction	Avoid
Rilpivirine	Preferably avoid combination; Use rifabutin instead of rifampicin. In treatment-naïve individuals RAL 800 mg bid may be considered	No significant interaction
Cationic antacids, calcium and iron supplements	Administer RAL 2 hours before, or 6 hours after	Administer DTG 2 hours before, or 6 hours after
Rifampicin	Preferably avoid combination; use rifabutin instead of rifampicin. In treatment-naïve individuals RAL 800 mg bid may be considered	Increase DTG dose to 50 mg bid
Rifabutin	No significant interaction	No significant interaction
Carbamazepine, Phenytoin	Unknown	Avoid

- The half-life of RAL necessitates twice-daily dosing whereas DTG can be administered as a single daily dose.

Resistance

Understanding RAL and DTG resistance mechanisms can help optimize their clinical use. Resistance has been well-described for all INSTI's but occurs more readily with RAL and Elvitegravir (which largely share resistance profiles) than DTG. The primary factors driving INSTI resistance are poor patient adherence and the prescription of suboptimal medication combinations.

Major Primary INSTI Resistance Mutations									
	T	E	E	G	Y	Q	N		
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Mutations in **ORANGE** associated with highest levels of reduced susceptibility or response.
Mutations in **YELLOW** reduce INSTI susceptibility or response.

Adapted from the Stanford HIV Drug Resistance Database.

Treatment failure within the first 6–12 months of RAL use is typically associated with the emergence of the N155H mutation, with or without secondary mutations. Viruses harboring this primary mutation are usually susceptible to DTG, permitting sequential use. In these cases, DTG at the higher dose of 50 mg bid should be prescribed as treatment.

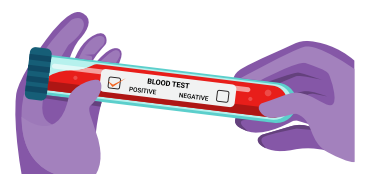
Failure after 12 months of RAL use is frequently due to the emergence of viruses that harbor the Q148H/R/K mutation, with or without secondary mutations. These viruses are invariably resistant to DTG as well. When DTG is used as the first INSTI, emergence of resistant viral populations is rare. The Q148H/R/K mutation markedly impairs viral fitness.

Testing for integrase inhibitor resistance

With the start of the use of INSTIs in South Africa, there will be the inevitable development of INSTI resistance. As a result of this, Lancet Laboratories have developed and validated an **Integrase Inhibitor Resistance Assay**.

Requirements for the Integrase Inhibitor Resistance Assay:

- The individual must be experiencing virological failure (HIV-1 viral load greater than 1 000 copies/mL)
- The individual must be taking the INSTI at the time of ordering the HIV Integrase Resistance Test
- Please state clearly on the request form that HIV Integrase resistance testing should be included as it does not form part of the normal, routine HIV resistance test
- Two EDTA (purple top) tubes are required



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ALL ABOUT HIV

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HIV testing tells you whether or not you have HIV. Knowing your status is important because it helps you make decisions to stay healthy and prevent getting or transmitting HIV.

Can you get tested for HIV?

Most HIV tests use a blood sample, either from a blood draw or a finger prick, but some use oral fluid or urine. Tests that use blood are even more accurate than other tests. Some test results are ready within 20 minutes, but others take a few days, depending on the type of test. work check

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A pregnant woman not treated with the proper drugs, has a **20-45% chance** that her infant will contract the virus from pregnancy. 59% of **HIV-positive people** in Africa are women, the majority of children diagnosed with HIV **get the virus from their mothers.**

DID YOU KNOW?

HIV can only be passed from person to person by exchanging bodily fluids. This most frequently happens during sex or when sharing needles.



What can you do if you are HIV positive?

It is essential to know your HIV status, especially if you are sexually active. It is advisable to test once every year.

Sexually active gay and bisexual men may benefit from more frequent testing (every 3 to 6 months).

Before having sex for the first time with a new partner, you and your partner should talk about your sexual and drug-use history, tell each other and then consider getting tested for HIV.

Are You at risk to HIV/AIDS?

Consult your health-care provider so they can advise you on the window period for the test you're taking. If you're using a self-test, read the test's package to understand your test result. If you get an HIV test within 3 months after a potential HIV exposure and the result is negative. However, do get tested again.

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Also, anyone who has been sexually assaulted should get an HIV test as soon as possible. (After reporting the assault.)

Which HIV test to do and why?

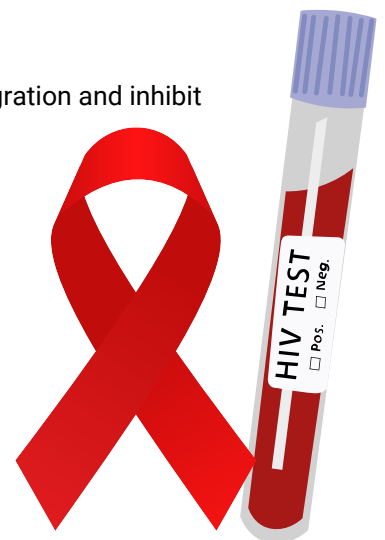


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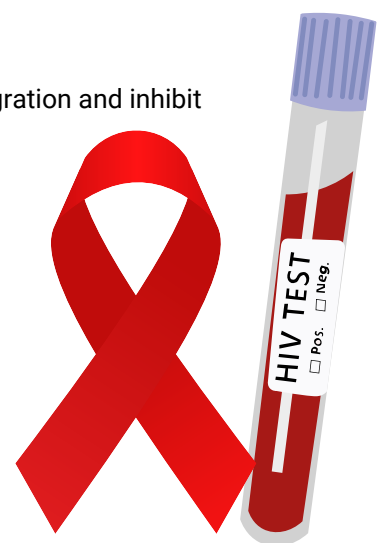


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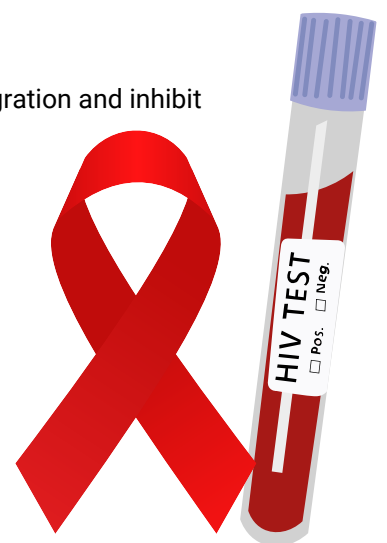


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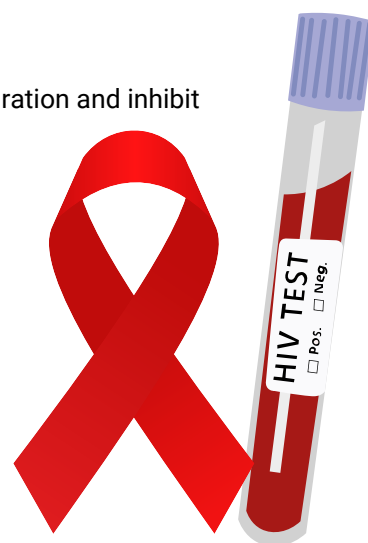


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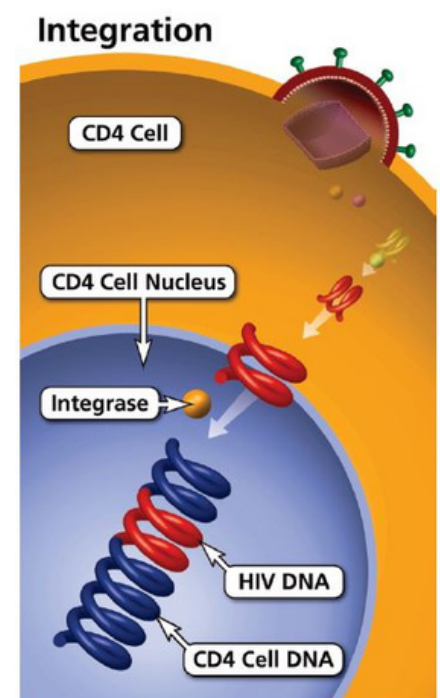
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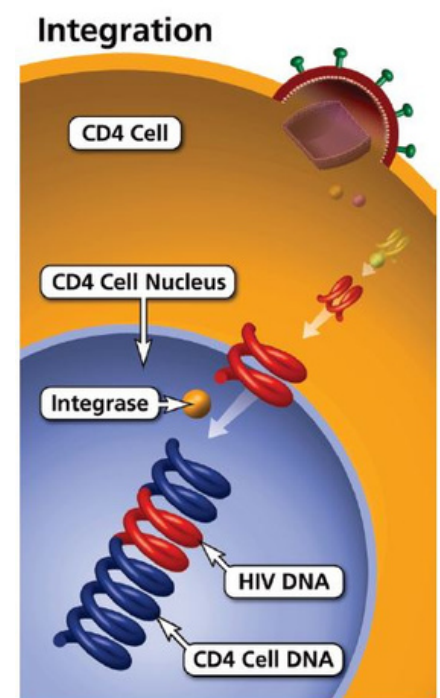
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Newsletter



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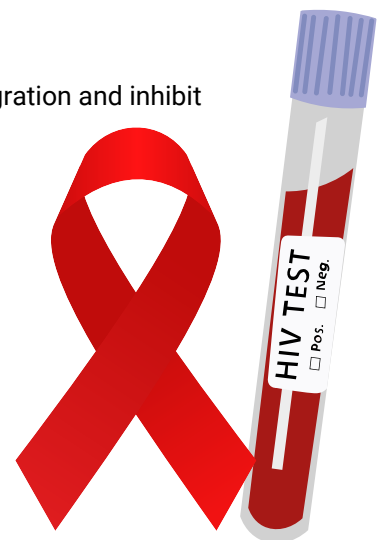


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Compiled by Dr C Wallis & Dr S Miller

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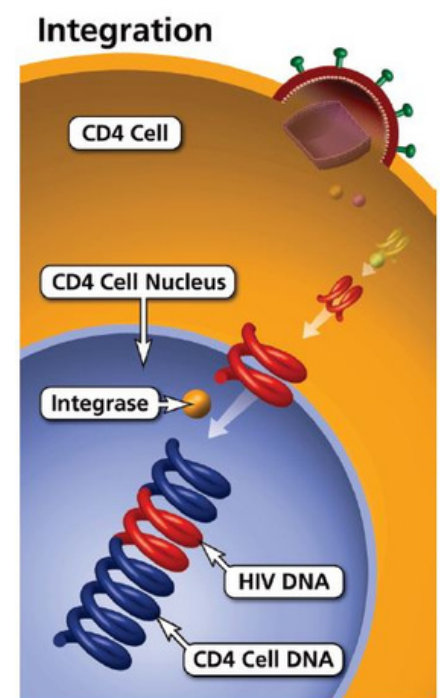
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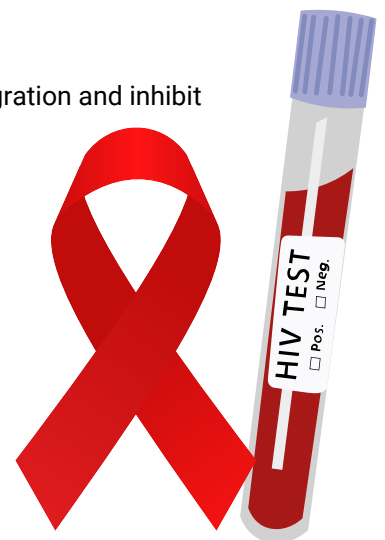


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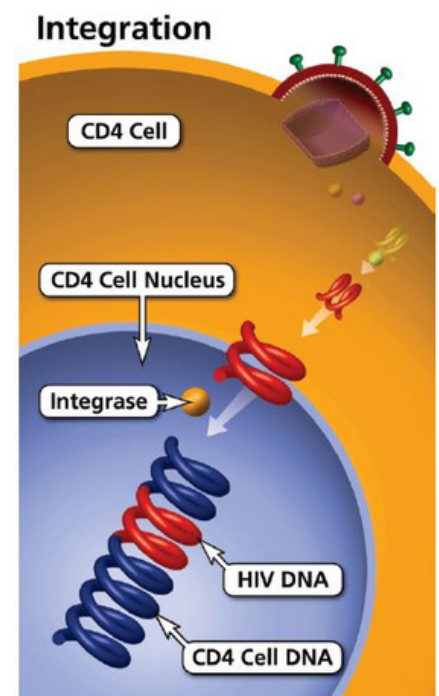
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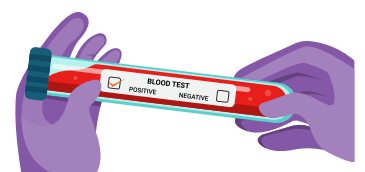
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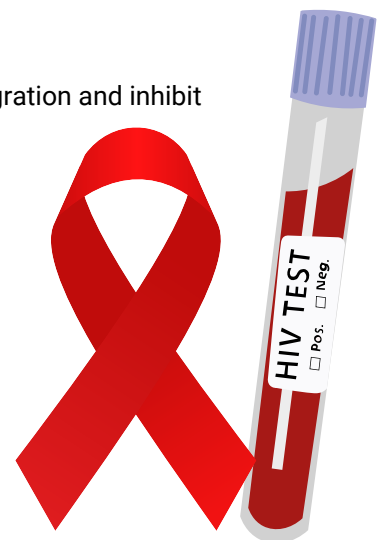


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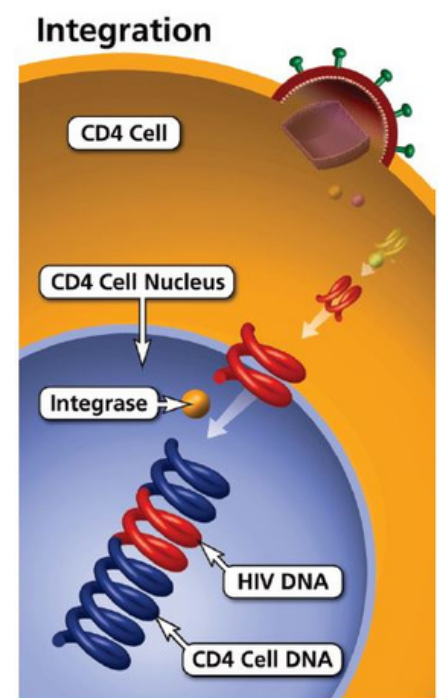
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Integrase strand transfer inhibitors, often abbreviated to "integrase inhibitors", target an enzyme called Integrase, a protein essential for HIV replication. As a result, proviral DNA is unable to insert into the host cell genome. This terminates the life cycle of the virus (see figure on the right).

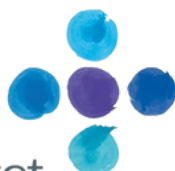
Three INSTI's have been approved by the FDA: Raltegravir (Isentress), Dolutegravir (Tivicay) and elvitegravir (Vitekta). Raltegravir (RAL) and Dolutegravir (DTG) is registered and available for routine use in South Africa and will be the focus of this clinical update.



Pharmacokinetics

Integrase inhibitors are well absorbed from the upper gastrointestinal tract, and rapidly achieve plasma levels that inhibit viral replication. The antiviral activity of INSTI's is primarily related to trough levels. These are usually well maintained with routine dosing regimens and are largely unaffected by concomitant food ingestion. The HIV-1 viral load declines rapidly using fully active regimens that include an INSTI; a significant proportion of individuals achieve a viral load of < 50 copies/mL within 4 weeks of commencing therapy.

RAL and DTG are primarily metabolized by Glucuronidation in the liver. There is minimal renal elimination; therefore, no dosage adjustment is necessary in patients with renal impairment. Data, however, are lacking on the use of RAL and DTG in individuals on renal dialysis and patients with severe hepatic impairment.



Clinically significant drug interactions

AGENT	RALTEGRAVIR	DOLUTEGRAVIR
Efavirenz	No significant interaction	No significant interaction
Etravirine	No significant interaction	Avoid
Nevirapine	No significant interaction	Avoid
Rilpivirine	Preferably avoid combination; Use rifabutin instead of rifampicin. In treatment-naïve individuals RAL 800 mg bid may be considered	No significant interaction
Cationic antacids, calcium and iron supplements	Administer RAL 2 hours before, or 6 hours after	Administer DTG 2 hours before, or 6 hours after
Rifampicin	Preferably avoid combination; use rifabutin instead of rifampicin. In treatment-naïve individuals RAL 800 mg bid may be considered	Increase DTG dose to 50 mg bid
Rifabutin	No significant interaction	No significant interaction
Carbamazepine, Phenytoin	Unknown	Avoid

- The half-life of RAL necessitates twice-daily dosing whereas DTG can be administered as a single daily dose.



Resistance

Understanding RAL and DTG resistance mechanisms can help optimize their clinical use. Resistance has been well-described for all INSTI's but occurs more readily with RAL and Elvitegravir (which largely share resistance profiles) than DTG. The primary factors driving INSTI resistance are poor patient adherence and the prescription of suboptimal medication combinations.

Major Primary INSTI Resistance Mutations									
	T	E	E	G	Y	Q	N		
Raltegravir	66	92	138	140	143	148	155		
	A	Q	KA	SA	RCH	HRK	H		
Elvitegravir	66	92	138	140		147	148	155	
	IAK	Q	KA	SA		G	HRK	H	
Dolutegravir		92	138	140			148		263
		Q	KA	SA			HRK		K

Mutations in **ORANGE** associated with highest levels of reduced susceptibility or response.
Mutations in **YELLOW** reduce INSTI susceptibility or response.

Adapted from the Stanford HIV Drug Resistance Database.

Treatment failure within the first 6–12 months of RAL use is typically associated with the emergence of the N155H mutation, with or without secondary mutations. Viruses harboring this primary mutation are usually susceptible to DTG, permitting sequential use. In these cases, DTG at the higher dose of 50 mg bid should be prescribed as treatment.

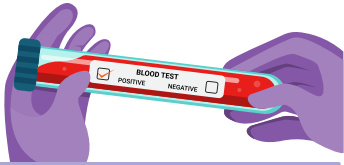
Failure after 12 months of RAL use is frequently due to the emergence of viruses that harbor the Q148H/R/K mutation, with or without secondary mutations. These viruses are invariably resistant to DTG as well. When DTG is used as the first INSTI, emergence of resistant viral populations is rare. The Q148H/R/K mutation markedly impairs viral fitness.

Testing for integrase inhibitor resistance

With the start of the use of INSTIs in South Africa, there will be the inevitable development of INSTI resistance. As a result of this, Lancet Laboratories have developed and validated an **Integrase Inhibitor Resistance Assay**.

Requirements for the Integrase Inhibitor Resistance Assay:

- The individual must be experiencing virological failure (HIV-1 viral load greater than 1 000 copies/mL)
- The individual must be taking the INSTI at the time of ordering the HIV Integrase Resistance Test
- Please state clearly on the request form that HIV Integrase resistance testing should be included as it does not form part of the normal, routine HIV resistance test
- Two EDTA (purple top) tubes are required



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Cerba Lancet
Africa

Newsletter



ALL ABOUT HIV

Compiled by: Centers for Disease & Control Prevention (CDC)



What is HIV ?

HIV testing tells you whether or not you have HIV. Knowing your status is important because it helps you make decisions to stay healthy and prevent getting or transmitting HIV.

Can you get tested for HIV?

Most HIV tests use a blood sample, either from a blood draw or a finger prick, but some use oral fluid or urine. Tests that use blood are even more accurate than other tests. Some test results are ready within 20 minutes, but others take a few days, depending on the type of test. work check

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A pregnant woman not treated with the proper drugs, has a **20-45% chance** that her infant will contract the virus from pregnancy. 59% of **HIV-positive people** in Africa are women, the majority of children diagnosed with **HIV get the virus from their mothers.**

DID YOU KNOW?

HIV can only be passed from person to person by exchanging bodily fluids. This most frequently happens during sex or when sharing needles.



What can you do if you are HIV positive?

It is essential to know your HIV status, especially if you are sexually active. It is advisable to test once every year.

Sexually active gay and bisexual men may benefit from more frequent testing (every 3 to 6 months).

Before having sex for the first time with a new partner, you and your partner should talk about your sexual and drug-use history, tell each other and then consider getting tested for HIV.



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[in](#) : Cerba Lancet Africa

Are You at risk to HIV/AIDS?

Consult your health-care provider so they can advise you on the window period for the test you're taking. If you're using a self-test, read the test's package to understand your test result. If you get an HIV test within 3 months after a potential HIV exposure and the result is negative. However, do get tested again.

If you think you've recently been exposed to HIV during sex (e.g. if the condom breaks or comes off) or through sharing needles, syringes or other injection equipment (for example, cookers), seek medical advice or see your doctor right away so they can let you know about post-exposure prophylaxis (PEP.) Remember to start PEP within 72 hours (3 days) of a possible exposure, but the sooner you start PEP, the better.

Also, anyone who has been sexually assaulted should get an HIV test as soon as possible. (After reporting the assault.)

Which HIV test to do and why?

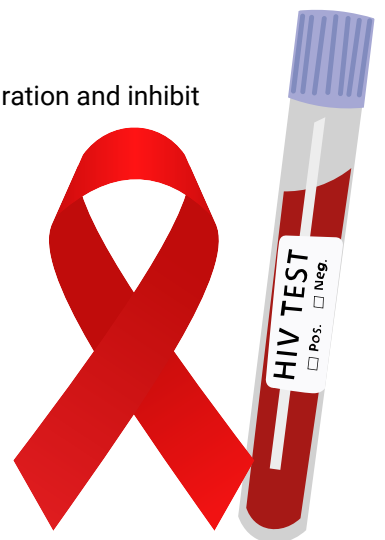


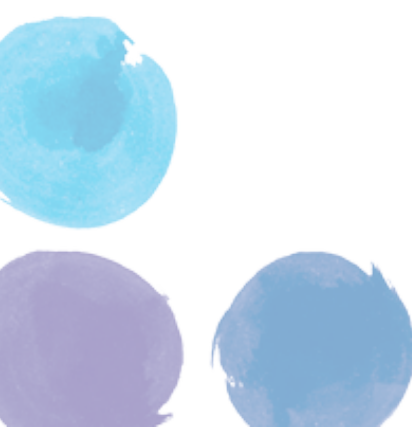
An antigen/antibody test looks for both HIV antibodies and antigens. Most laboratory tests are antigen/antibody tests. Antigens are foreign substances that cause your immune system to activate. The antigen is part of the virus itself and is present during the early stage of HIV infection (called acute infection). If you have HIV, an antigen called p24 is produced even before antibodies develop. A rapid antigen/antibody test is available.

Nucleic acid tests (NAT) look for HIV in the blood. The NAT can give either a positive/negative result or the actual amount of virus present in the blood (known as a viral load test). This test is very expensive and not routinely used for screening individuals unless they recently had a high-risk exposure or they had a possible exposure and have early symptoms of HIV infection.

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3. HIV Prevention | Let's Stop HIV Together | CDC
4. HIV Risk Reduction Tool | CDC





Newsletter

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How to create an eating plan for type 2 Diabetes?

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This is the most common type of Diabetes. People with this type of diabetes do not make enough insulin and/or the body's cells do not respond to insulin. Therefore, they need to take tablets to help the body to make more insulin or that help insulin to do its job; or they may need to take insulin injections every day. People who are overweight and inactive have an increased risk of developing type 2 diabetes.

The likelihood of developing Diabetes is much higher if you:

- Low HDL (good cholesterol) and high levels of other lipids (fats)
- Had Diabetes during pregnancy and delivered a large baby (4 kg or more)
- A parent, sister or brother with Diabetes
- 40 years or older
- Overweight
- Black or Indian
- High blood pressure above 140/90 mmHg)



How to create an eating plan for type 2 Diabetes?

- Eat three balanced meals a day, not more than six hours apart.
- Limit added sugars and sweets.
- Eat a variety of vegetables and fruit each day.
- Eat your fruit rather than drinking it as juice.
- Include whole-grain starchy foods at each meal.
- Choose low-GI foods.
- Drink water instead of a fizzy or fruit drink.
- Always choose lean protein at each meal.
- Make low-fat choices and cut down on added-on fat, (butter, margarine and cheese).
- Include beans and lentils in your diet.
- Choose to drink alcohol only in moderation.
- Reduce your salt intake.



Complications with Diabetes

If Diabetes is not diagnosed early or is not adequately controlled, the risk of complications increases.

The following are some of the major complications of Diabetes:

- Kidney disease
- Eye disease that can lead to blindness
- Disease of the peripheral nerves
- Heart disease
- Stroke
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HbA1c Test

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Lipogram Test

Total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides form part of a standard lipogram. These lipids are used to estimate the risk of heart disease (E.g. Heart attack and Stroke).

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DIABETES

Compiled by Dr Shamin Mahabeer

What is Diabetes?

Diabetes is a lifelong disease in which the body cannot process sugar properly. Diabetes is also called "**diabetes mellitus**" or "**sugar diabetes**". When people who have diabetes eat glucose, which is found in foods such as breads, potatoes and sweets, it can't be converted into energy. Instead of being converted into energy, the glucose stays in the blood. This is why people who have diabetes have blood sugar. (**Glucose.**) that is too high. Your blood needs to always contain sugar as available energy but too much sugar is not good for your health as it may damage your heart, kidneys, eyes, nerves, teeth and gums.



There are two common types of Diabetes

Type 1 Diabetes

This is commonly diagnosed in children, teenagers and young adults. People with this type of diabetes do not produce **insulin** which is used by the **body to lower sugar levels in blood.** These patients need to take insulin injections every day.



Type 2 Diabetes

This is the most common type of diabetes. People with this type of diabetes do not make enough insulin and/or the body's cells do not respond to insulin. Therefore, they need to take tablets to help the body to make more insulin or that help insulin to do its job; or they may need to take insulin injections every day. People who are overweight and inactive have an increased risk of developing type 2 diabetes.

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Steps for COVID-19 Vaccination

1.

Line up at Hall A for confirmation of your vaccination slot. Please prepare your valid ID.

2.

Go to Hall B and wait until your name is called.

3.

You will then be taken to Hall C for your vaccination.



**Vaccinations will run
from 8 AM to 6 PM only.**

**Please maintain proper social
distancing while queuing.**

Newsletter

FATIGUE AND BIOLOGICAL ASSESSMENTS

Compiled by: Cerballiance Editorial Board

The different types of fatigue



Fatigue is the first reason for consultation with general practitioners. However, this general term covers very diverse origins, most often banal but sometimes more serious. Fatigue is to be differentiated from asthenia, a medical term, which corresponds to fatigue that is not improved by rest. Asthenia requires a consultation with your GP.

The very diverse realities of its symptoms thus require appropriate medical responses. Targeted biological analyses, prescribed by your doctor, and selected according to the problems experienced, can thus provide the first answers as to the origin of this fatigue or asthenia.

What do the terms fatigue and asthenia mean?

A frequent symptom, fatigue is the first reason for consultation with general practitioners. However, this term covers very diverse origins, most often banal, sometimes more serious. These very diverse realities require appropriate medical responses.

Often confused terms, fatigue is to be distinguished from asthenia. Unlike fatigue, asthenia does not diminish with rest. It is a set of symptoms whose cause is most often organic, that is to say, linked to a disease or be a sequel after an acute pathology (an infection for example). Appropriate biological analyses, selected according to the disorders experienced, can thus provide the first answers as to the origin of this fatigue.

DID YOU KNOW?

Even very young children may show early warning signs of mental health concerns. These mental health problems are often clinically diagnosable.

First step: talk to your Doctor

During a consultation with your doctor, he will first ask you questions to better understand the origin of the disorder, such as:

- **What time of day?**
- **Since when?**
- **For what occasion?**
- **What is your way of life?**
- **Is your fatigue more physical, psychological, or sexual?**
- **Do you have a background?**
- **Do you take any treatments?**
- **Do you have fever or weight loss?**

You may have one or more of the symptoms mentioned. It is advisable to visit your doctor so that he/she can decide on the appropriate test.

Analyzes in the medical analysis laboratory

If this questioning and auscultation cannot explain the origin of your fatigue, your doctor may prescribe a biological assessment generally including:

- Harmful side-effects associated with PSA screening. (E.g., Bleeding, Infection, Urinary incontinence are common.)
- The PSA test should be used for screening only after a detailed discussion with the patient, ideally with the use of decision aids to facilitate comprehension of the pros and cons of screening for Prostate Cancer. The American College of Physicians (ACP) recommends screening using PSA only in those patients who express a clear preference for the test or in patients identified as high risk after clinical evaluation¹³.
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ISO 15189:2012 ACCREDITED LABORATORY

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Analyzes in the medical analysis laboratory

If this questioning and auscultation cannot explain the origin of your fatigue, your doctor may prescribe a biological assessment generally including:

- Harmful side-effects associated with PSA screening. (E.g., Bleeding, Infection, Urinary incontinence are common.)
- The PSA test should be used for screening only after a detailed discussion with the patient, ideally with the use of decision aids to facilitate comprehension of the pros and cons of screening for Prostate Cancer. The American College of Physicians (ACP) recommends screening using PSA only in those patients who express a clear preference for the test or in patients identified as high risk after clinical evaluation¹³.
- To complete this assessment, a full range of specialized analyses can be carried out in our laboratories: vitamin assessment, oxidative stress assessment, etc. The biologists in our laboratories will be there to guide you.



1. Reference Source: <https://www.cerballiance.fr/fr/blog/prevention-nutrition/fatigue-et-bilans-biologiques>.

Newsletter

FATIGUE AND BIOLOGICAL ASSESSMENTS

Compiled by: Cerballiance Editorial Board

The different types of fatigue



Fatigue is the first reason for consultation with general practitioners. However, this general term covers very diverse origins, most often banal but sometimes more serious. Fatigue is to be differentiated from asthenia, a medical term, which corresponds to fatigue that is not improved by rest. Asthenia requires a consultation with your GP.

The very diverse realities of its symptoms thus require appropriate medical responses. Targeted biological analyses, prescribed by your doctor, and selected according to the problems experienced, can thus provide the first answers as to the origin of this fatigue or asthenia.

What do the terms fatigue and asthenia mean?

A frequent symptom, fatigue is the first reason for consultation with general practitioners. However, this term covers very diverse origins, most often banal, sometimes more serious. These very diverse realities require appropriate medical responses.

Often confused terms, fatigue is to be distinguished from asthenia. Unlike fatigue, asthenia does not diminish with rest. It is a set of symptoms whose cause is most often organic, that is to say, linked to a disease or be a sequel after an acute pathology (an infection for example). Appropriate biological analyses, selected according to the disorders experienced, can thus provide the first answers as to the origin of this fatigue.

First step: talk to your Doctor

During a consultation with your doctor, he will first ask you questions to better understand the origin of the disorder, such as:

- **What time of day?**
- **Since when?**
- **For what occasion?**
- **What is your way of life?**
- **Is your fatigue more physical, psychological, or sexual?**
- **Do you have a background?**
- **Do you take any treatments?**
- **Do you have fever or weight loss?**

You may have one or more of the symptoms mentioned. It is advisable to visit your doctor so that he/she can decide on the appropriate test.

DID YOU KNOW?

Even very young children may show early warning signs of mental health concerns. These mental health problems are often clinically diagnosable.



Analyzes in the medical analysis laboratory

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