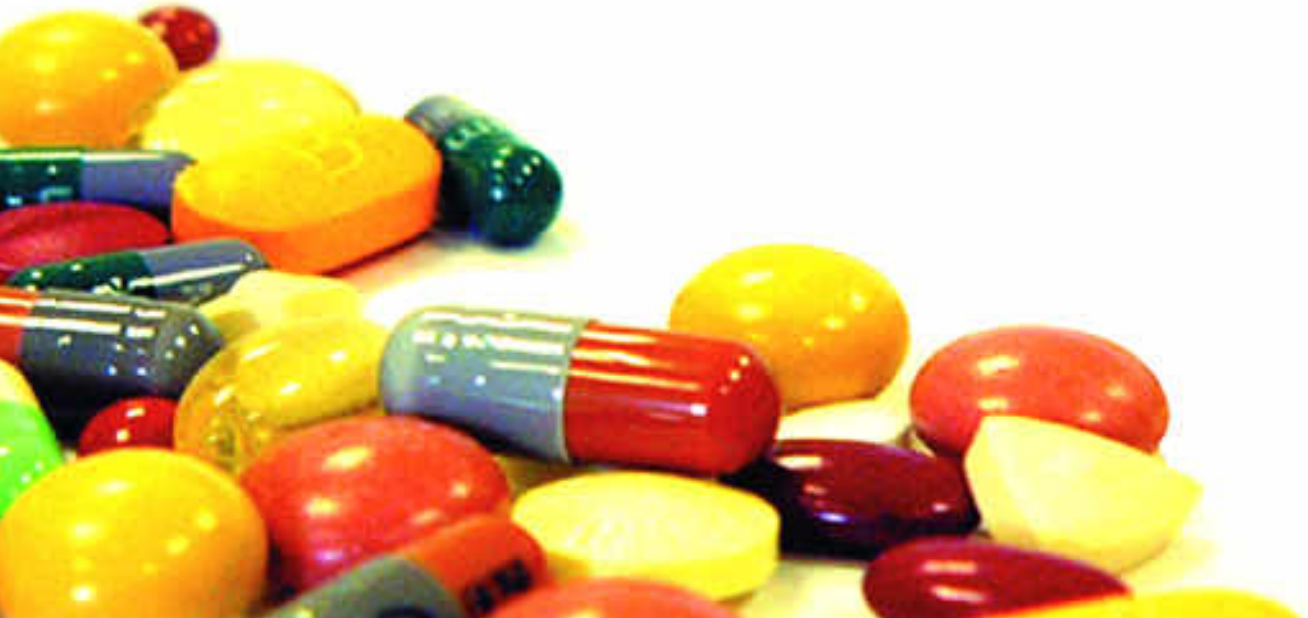
Information about HIV & AIDS Treatment

AVERT



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You can access more information on HIV/AIDS and treatment by going to HIV/AIDS treatment and care index page at http://www.avert.org/hivtreatment.htm

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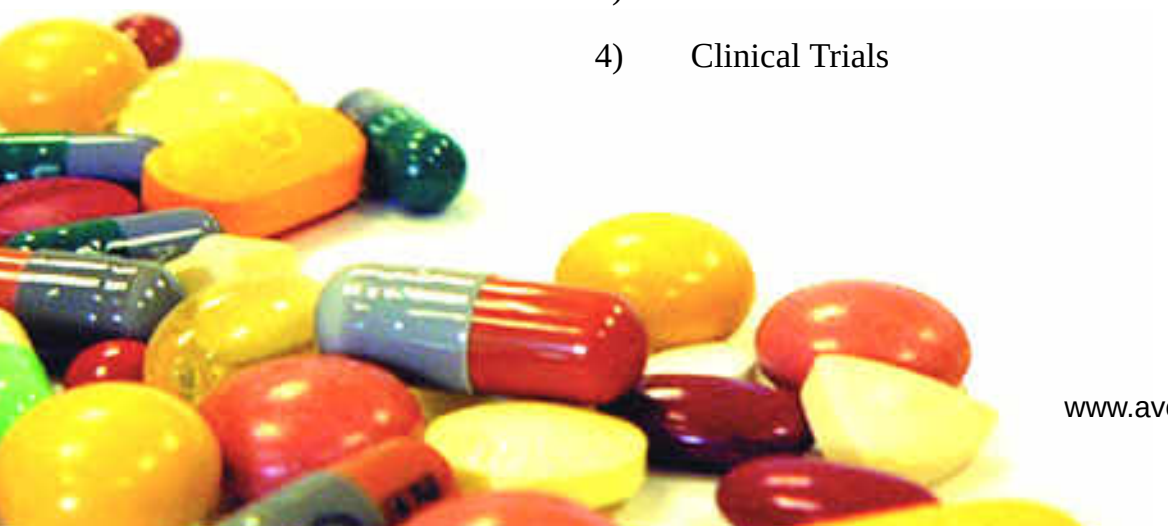


An Introduction to HIV/AIDS Treatment

What is HIV antiretroviral treatment?

This is the main type of treatment for HIV or AIDS. It is not a cure, but it can stop people from becoming ill for many years. The treatment consists of drugs that have to be taken every day for the rest of someone's life. To understand about treatment you need to have some knowledge of HIV and AIDS, and some basic information can be found at the end of this booklet (pages 30 - 31).

HIV is a virus and like other viruses, when it is in a cell in the body it produces new copies of itself. With these new copies, HIV can go and infect other previously healthy cells. It is easy for HIV to spread quickly through the billions of cells in the body, if it is not stopped from reproducing itself. Antiretroviral treatment for HIV infection consists of drugs which work against HIV infection itself by slowing down the reproduction of HIV in the body. The drugs are often referred as:

- antiretrovirals
- anti-HIV drug
- HIV antiviral drugs

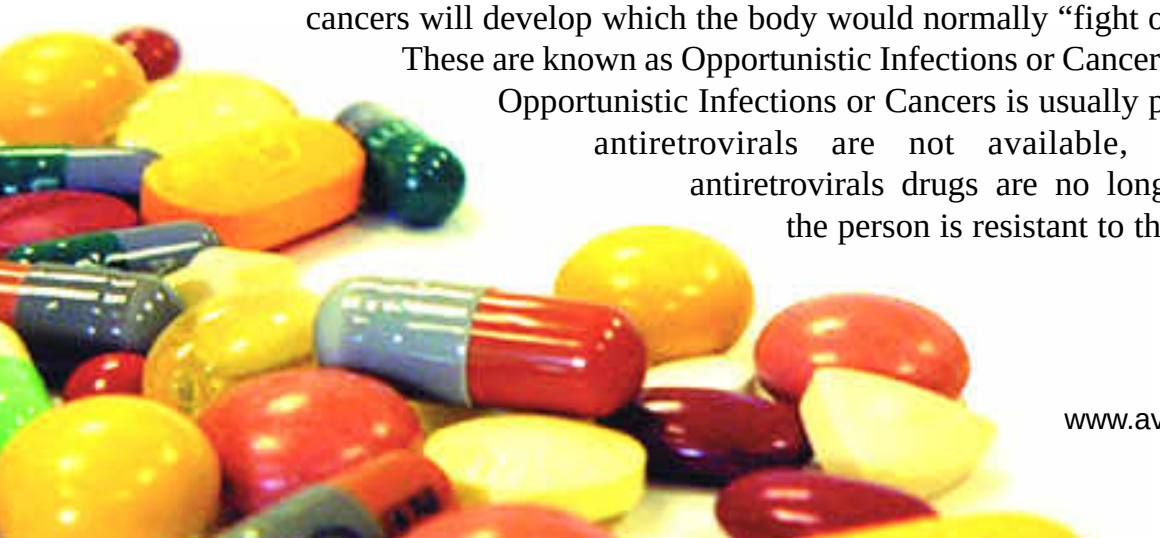
What is Combination Therapy, what is HAART?

For antiretroviral treatment to be effective for a long time, it has been found that you need to take more than one antiretroviral drug at a time. This is what is known as Combination Therapy. The term Highly Active Antiretroviral Therapy (HAART) is used to describe a combination of three or more anti-HIV drugs.

The general recommendation is to use a minimum of three antiretroviral drugs. If one drug is taken on its own, it has been found that, over a period of time, the drug stops working. HIV reacts to the drug in the person's body and changes, so that the virus is no longer affected by the drug. The virus then starts to reproduce itself the same way as before. This is known as the virus becoming resistant to the drug. If two or more antiretrovirals are taken together it vastly reduces the rate at which resistance develops. There is more about resistance later in the booklet (pages 11 - 13).

The Treatment of Opportunistic Infections

When a person's immune system is damaged by HIV, then certain infections or cancers will develop which the body would normally "fight off" quite easily. These are known as Opportunistic Infections or Cancers. Treatment for Opportunistic Infections or Cancers is usually provided when antiretrovirals are not available, or when the antiretrovirals drugs are no longer effective as the person is resistant to them.



The Groups of Antiretroviral Drugs

There are three main groups of anti-HIV drugs. Each of these groups attacks HIV in a different way.

Reverse Transcriptase Inhibitors

HIV needs an enzyme called reverse transcriptase in order to be able to infect healthy cells and reproduce itself in a person's body. As the name says, reverse transcriptase inhibitors slow down the production of the reverse transcriptase enzyme and make HIV unable to infect cells and duplicate itself.

The Reverse Transcriptase Inhibitors are divided into three sub groups.

a) Nucleoside Reverse Transcriptase Inhibitors

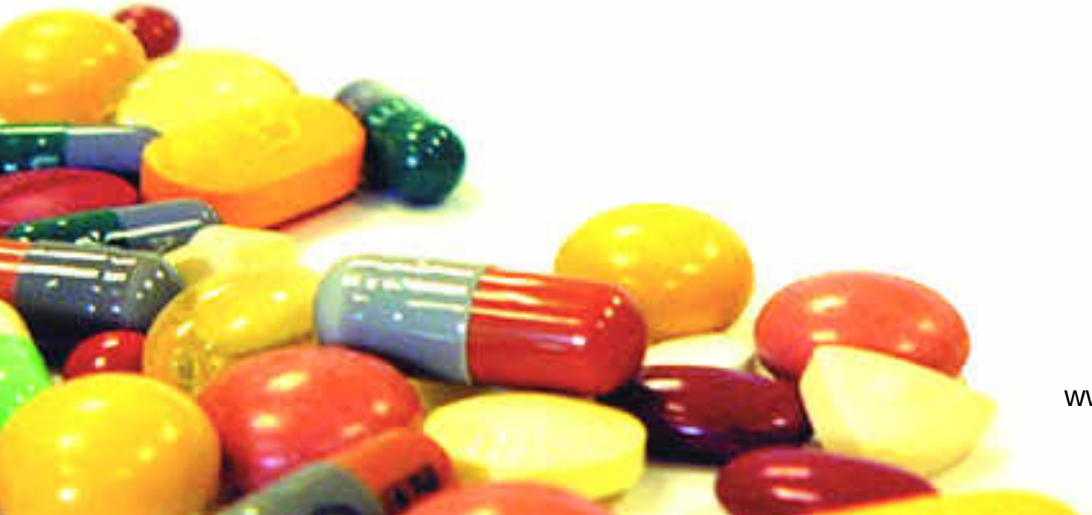
The Nucleoside Reverse Transcriptase Inhibitors (NRTIs) were the first type of drug available to treat HIV infection in 1987. They are better known as nucleoside analogues or nukes.

b) Non-Nucleoside Reverse Transcriptase Inhibitors

The Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) started to be approved in 1997 and are generally referred as non-nucleosides or non-nukes. This group of drugs also stops HIV from infecting cells by intervening with the trancriptase enzyme of the virus. The non-nucleoside drugs work slightly differently from the nucleoside analogues in that they bind in a different way to the cell's reverse transcriptase.

c) Nucleotide Reverse Transcriptase Inhibitors

There is currently one Nucleotide Reverse Transcriptase Inhibitor drug, Tenofovir. It also works by inhibiting the Reverse Transcriptase enzyme, but it works in a slightly different way to the other Reverse Transcriptase Inhibitors.



Protease Inhibitors

The second type of antiretroviral is the Protease Inhibitor (PI) group. They were first approved in 1995. Protease inhibitors, as the name says, inhibit protease. Protease is a digestive enzyme that breaks down protein and is one of the many enzymes that HIV uses to reproduce itself. The protease in HIV attacks the long healthy chains of enzymes and proteins in the cells and cuts them into smaller pieces. These infected smaller pieces of proteins and enzymes continue to infect new cells. The protease inhibitors take effect before the protease in HIV has the chance to break down the protein and enzymes. This way the protease inhibitors slow down the duplication of the virus and thus prevent the infection of new cells.

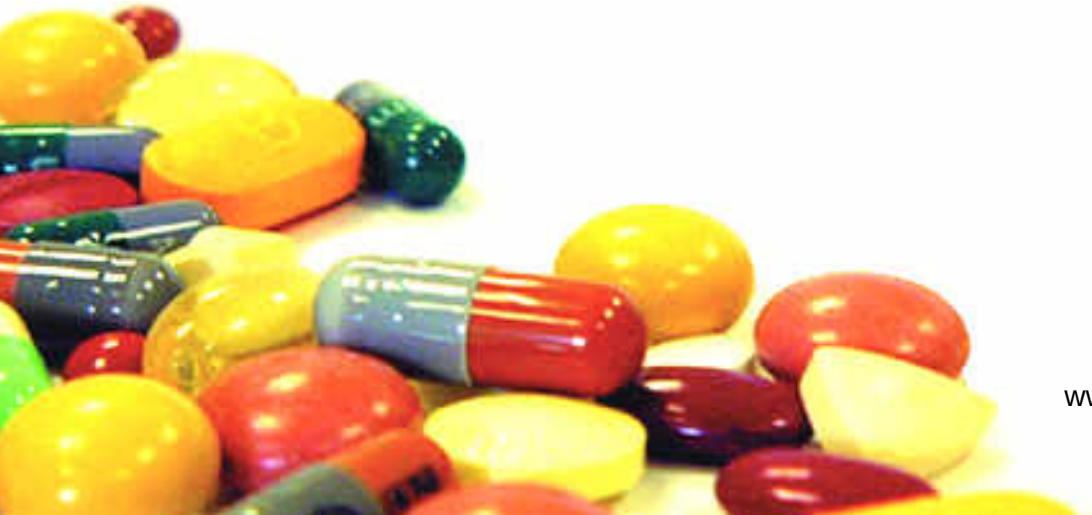
Protease inhibitors are able to slow the process of immature non-infectious virus becoming mature and infectious. Protease inhibitors also work in cells that have been infected for a long time, by slowing down the reproduction of the virus.

Fusion or Entry Inhibitors

The third group of antiretrovirals are called Fusion or Entry Inhibitors.

The surface of HIV carries proteins called gp41 and gp120. These are the proteins which allow HIV to attach itself to, and enter into cells. By blocking one of these proteins, fusion inhibitors slow down the reproduction of the virus. For example, T-20, the fusion inhibitor that is closest to approval, sticks to the protein gp41.

The T-20 Fusion Inhibitor differs from other antiretrovirals in that it needs to be injected. T-20 is a protein and cannot be taken orally, since it would be digested in the stomach.



The Names of the Antiretroviral Drugs

There are currently 20 approved antiretroviral drugs in the UK and many more in the expanded access programmes and trials. Each antiretroviral drug usually has three names. Sometimes drugs are referred by their research or chemical name, for example AZT. The second name for the drug is the common name for all the drugs with the same chemical structure, for example AZT is also known as zidovudine. The third name is the brand name given by the pharmaceutical company. One of the brand names for zidovudine is Retrovir. The brand name may not be the same in every country.

The drug names listed here are those that are most commonly used. Those with * are not yet approved but are available on an expanded access programme. This list does not contain new drugs that are currently under development and still in clinical trials. Further information should be available from your doctor.

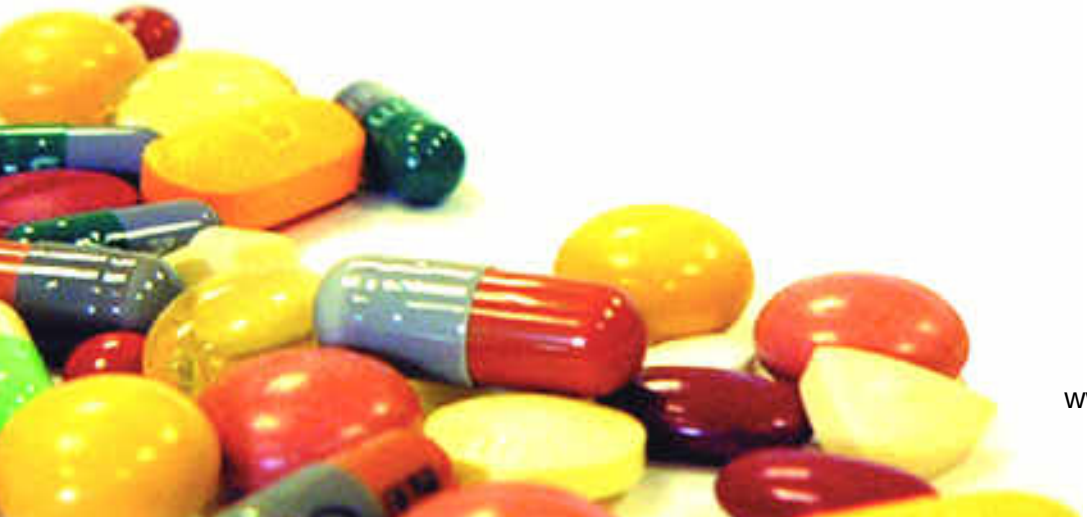
Reverse Transcriptase Inhibitors

Nucleoside Analogues (NRTIs)

Name	**Brand & Other names**
3TC	Epivir, lamivudine
Abacavir	Ziagen, ABC
AZT	Retrovir, zidovudine
Combivir	(AZT/3TC combined)
Trizivir !	(AZT/3TC/abacavir combined)
d4T	Zerit, stavudine
ddC	Hivid, zalcitabine
ddI	Videx (tablet) Videx EC (capsule), zalcitabine
FTC	Emtriva, emtricitabine

Non-Nucleoside Reverse Transcriptase inhibitors (NNRTIs)

delavirdine*	Rescriptor
efavirenz	Sustiva
nevirapine	Viramune



Nucleotide Reverse Transcriptase inhibitors

Tenofovir	Viread

Protease Inhibitors (PIs)

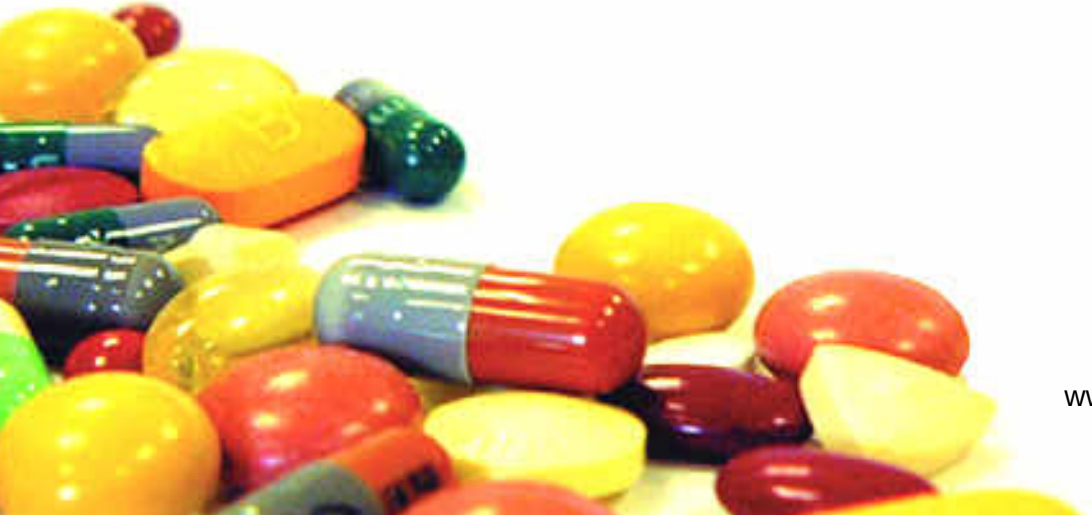
amprenavir	Agenerase
atazanavir	Reyataz
indinavir	Crixivan
lopinavir/ritonavir	Kaletra
nelfinavir	Viracept
ritonavir	Norvir
saquinavir	Fortovase (soft gel) Invirase (hard gel)
Tipranavir*	PNU-140690

Fusion or Entry inhibitors

T-20 !!	Fuzeon, Enfuvirtide

! British HIV Association (BHIVA) recommends that Trizivir should only be considered as a starting regimen in special situations, for example informed patient choice based on likely poor adherence if alternative options are used, or concomitant medication such as for TB.

!! T-20 is approved for use in individuals who have experienced failure of drugs from each existing class of antiretrovirals, or who have intolerance to previous antirectroviral regimens. T-20 should be reserved for salvage use in combination with one or preferably two other new drugs that are expected to be active on the basis of resistance data, to give a realistic prospect of suppressing viral replication completely (UK).



Tests

There are certain tests which can give you information that can help you to decide about treatment, in particular the CD4 test and the viral load test. There are also other tests such as resistance testing and therapeutic drug monitoring (TDM) that can help determine how well your treatment is working. You can read more about resistance testing and TDM later on in this booklet.

The CD4 Test

The main cell HIV attacks is called a T-helper cell or CD4 cell. The T-helper cell plays an important part in the immune system. It helps to co-ordinate all the other cells to fight illnesses. Any damage to T-helper cells can have a serious effect on the immune system.

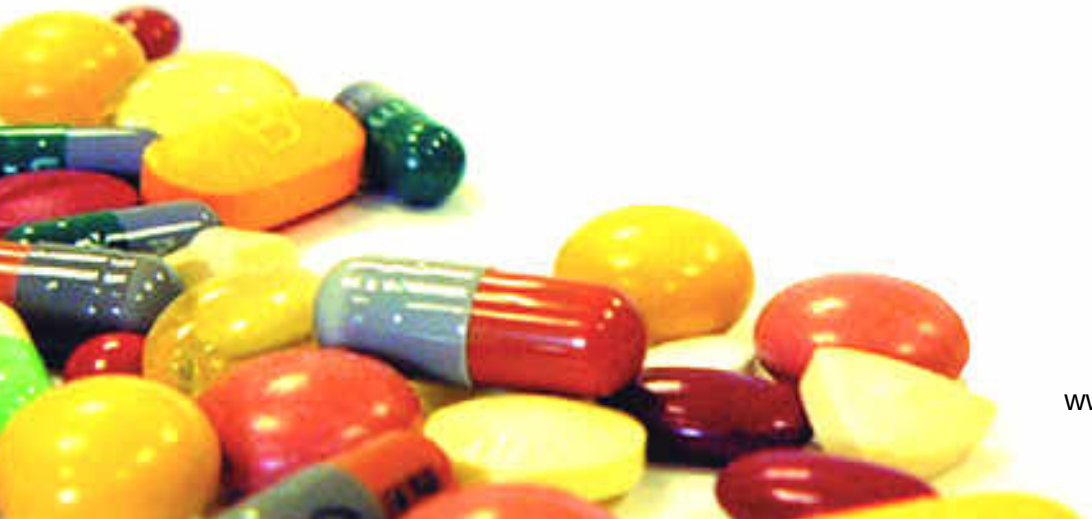
The T-helper cell has a protein CD4 on its surface. HIV needs the CD4 in order to enter the cells it targets to infect. If HIV is able to enter the T-helper cell, it can take over the cell and then use it to duplicate itself. When HIV produces more copies of itself, the amount of CD4 cells decreases. As a result, there are fewer cells available to help the immune system to fight illnesses.

The CD4 test measures the number of CD4 or T-helper cells in your blood. The more CD4 cells in your blood you have per millimetre, the stronger is your immune system. The stronger the immune system, the better the body can fight illnesses.

The Viral Load Test

The viral load refers to the amount of HIV in your blood. The result of a viral load test indicates how much virus there is in the blood and which can harm the immune system.

The higher the level of HIV in your blood, the faster your CD4 cells are being destroyed by HIV. The lower the viral load, the stronger is your immune system. The result of the viral load test is normally described as the amount of HIV RNA copies per millimetre of blood.



A viral load test can provide important information about the likely course of HIV infection. There are different viral load tests available. Each of them uses a different technique to measure the amount of HIV in the blood. All the tests are equally reliable at determining the viral load. The results from the different tests tell you whether the viral load is low medium or high. A viral load higher than 100,000 copies is considered to be high, and below 10,000 is considered low in people who are HIV positive.

Sometimes the viral load is so low that it cannot be measured. This is called an undetectable viral load. It does not mean that the person does not have any HIV in the blood or is not infected with HIV any more. An undetectable viral load indicates that the level of HIV is too low to be measured by the viral load test. The tests in the past were only able to measure the viral load as low as 400 or 500 copies. Now, in some places ultrasensitive viral load tests are available that can measure down to 50 copies.

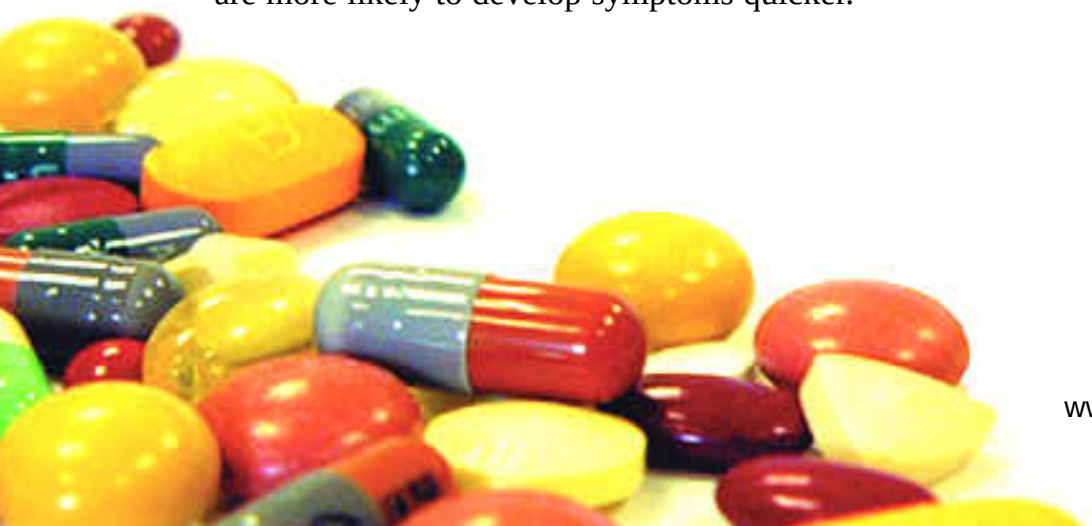
The advantages of having undetectable viral load are that the person has lower risk of developing AIDS and also a low risk of developing resistance to the drugs if taking anti-HIV drugs.

Understanding the Test Results

The results of the CD4 count and the viral load test can provide you with valuable information. The combination of the results may help to predict the course of the HIV infection and the likehood of possible illnesses.

The CD4 test can provide you with information about the overall health of the immune system - whether it is staying the same, improving or declining. Sometimes things like stress, infections, exercise, menstrual cycle and smoking can have an affect to the result. That is why it is more important to concentrate on the overall trend of the test results rather than individual tests,

The viral load and CD4 count also interact with each other, and it is therefore important to monitor both regularly. Some studies have shown that people with the same CD4 count but who have a higher viral load are more likely to develop symptoms more quickly than those with a lower viral load. It has also been suggested that people with the same viral load but those with lower CD4 counts are more likely to develop symptoms quicker.



Drug Resistance

Antiretroviral drugs slow down the reproduction of HIV in the body. But the drugs cannot stop the reproduction of HIV completely, and so some HIV is able to survive despite on-going treatment.

HIV reproduces itself very quickly and when reproducing often makes slight mistakes. So each new generation, or new strain, of HIV differs slightly from the one before. These tiny differences in the structure of HIV are called mutations. Some of the mutations occur in the parts of HIV, which are targeted by anti-HIV drugs. So although you have some HIV that continues to be affected by the drugs, you have other strains of HIV that are not affected by the anti-HIV drugs as effectively as before. This HIV is called drug resistant HIV, and it is then able to reproduce unaffected by the drugs.

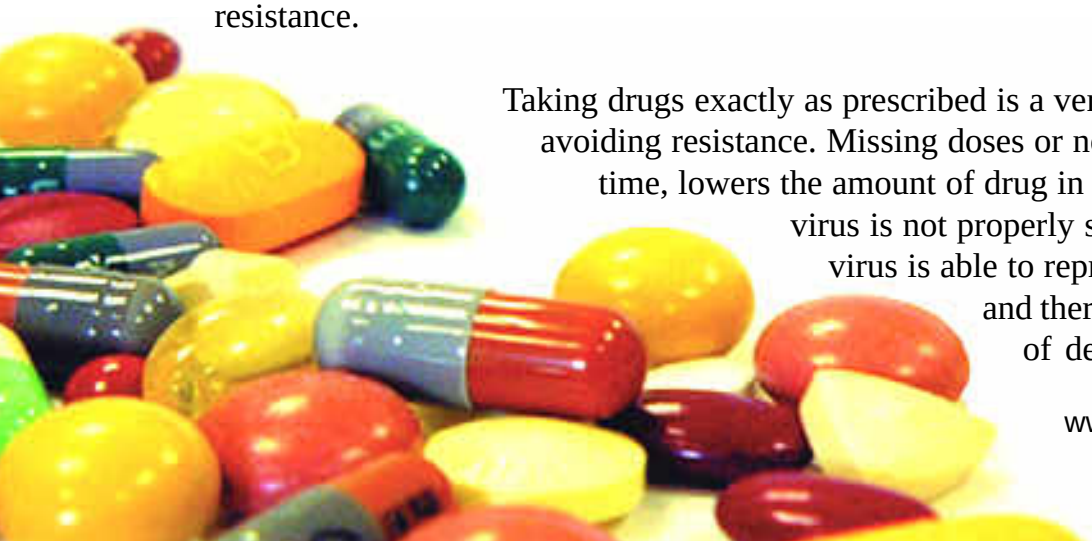
When someone has drug resistant HIV (commonly referred to as drug resistance), the amount of HIV in the blood rises and the risk of the person becoming ill increases. Drug resistance is one of the main reasons why antiretroviral treatment fails. If resistance to the current drug treatment is developed, this usually means that the drug regime needs to be changed.

The viral load test can reveal developing drug resistance. Normally when treatment is started, the viral load drops to the undetectable level. A sign of developing resistance is if the viral load increases. In some countries, the resistance to certain drugs can be monitored by using specific resistance testing: genotypic and phenotypic testing.

Avoiding resistance

There are certain things that can be done to minimalise the risk of developing drug resistant HIV. If the drug combination is strong, and HIV is not able to mutate, there is less risk of resistance developing. This often means taking a combination of 3 or 4 drugs.

Regular viral load testing. The viral load test can indicate if you are developing a drug resistant strain of HIV. If the drug combination is working, the viral load should be undetectable. If the viral load has increased, this can be a sign of growing drug resistance.



Taking drugs exactly as prescribed is a very important part of avoiding resistance. Missing doses or not taking them on time, lowers the amount of drug in your body and the virus is not properly suppressed. Then the virus is able to reproduce itself faster and there is an increased risk of developing resistance.

Cross-resistance

Developing resistance to some antiretroviral drugs can limit which treatment options are available to you in the future. If HIV is resistant to one drug, it will sometimes be resistant to similar drugs in the same group. This is called cross-resistance and it means that some anti-HIV drugs will not work even though you have not used them before.

Cross-resistance is a particular problem if a person develops cross-resistance to a whole group of drugs. For example, if a person has developed a resistance to one of the non-nucleoside drugs, there is a risk that none of the other non-nucleosides will be effective.

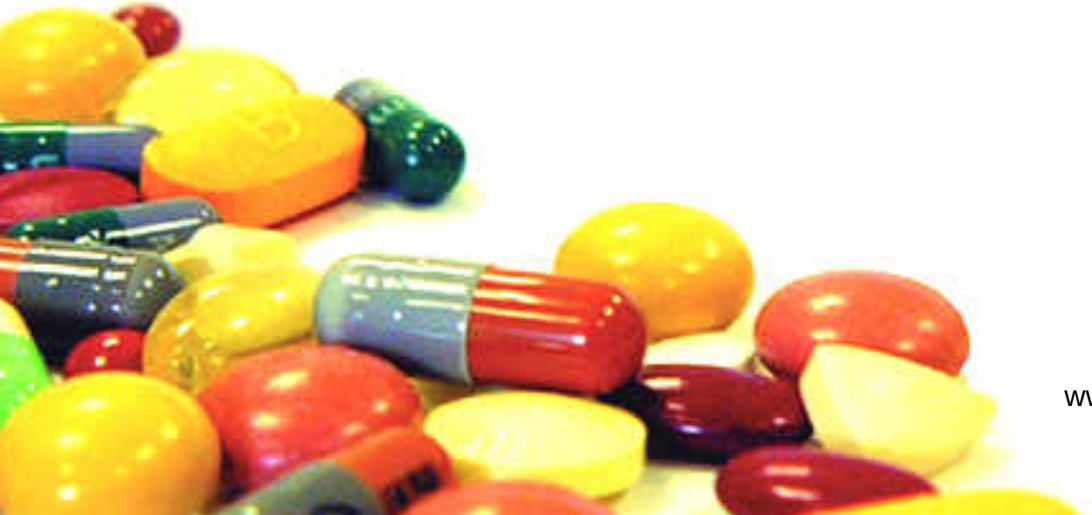
Infection with Drug-Resistant HIV

People can be infected with a drug-resistant strain of HIV. The wide use of antiretrovirals in the developed parts of the world, has caused drug-resistant strains of HIV to emerge. This is virus, which is already resistant to some antiretroviral drugs. Becoming infected with the drug-resistant HIV can limit the treatment options available to you.

Resistance Testing

There are certain blood tests that can detect whether the HIV in your body is resistant to certain antiretroviral drugs. Resistance testing is a recent development in HIV and is not available everywhere. However, resistance testing is becoming more common and cheaper.

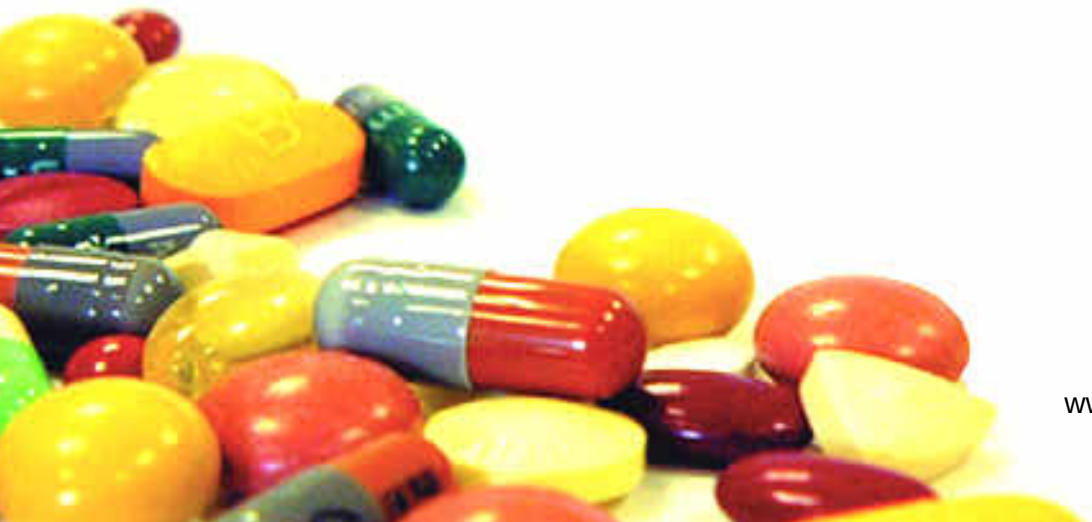
Resistance tests are particularly recommended to people whose anti-HIV treatment is failing. The test results can you help to choose the drugs in your next regimen. The test results should be considered alongside your treatment history because drug resistance is not the only reason why treatment sometimes fails.



There are two main ways of testing for HIV drug resistance: phenotypic and genotypic testing. Phenotypic testing measures the amount of a drug required to suppress the viral replication by a set amount. If resistance to that drug starts to grow, higher levels of that drug is needed to stop HIV replicating. Genotypic testing looks for the presence of genetic mutations, or changes, in HIV that may be associated with drug resistance.

There is no clear indication which type of testing is more useful. Both have their advantages and disadvantages. Overall, the tests are not good at detecting 'minor mutations' and work better when the viral load is higher.

The tests results can be difficult to understand and sometimes they don't explain what actually happens with you. Despite these problems, many researchers believe that resistance testing will soon become a standard part of HIV treatment.



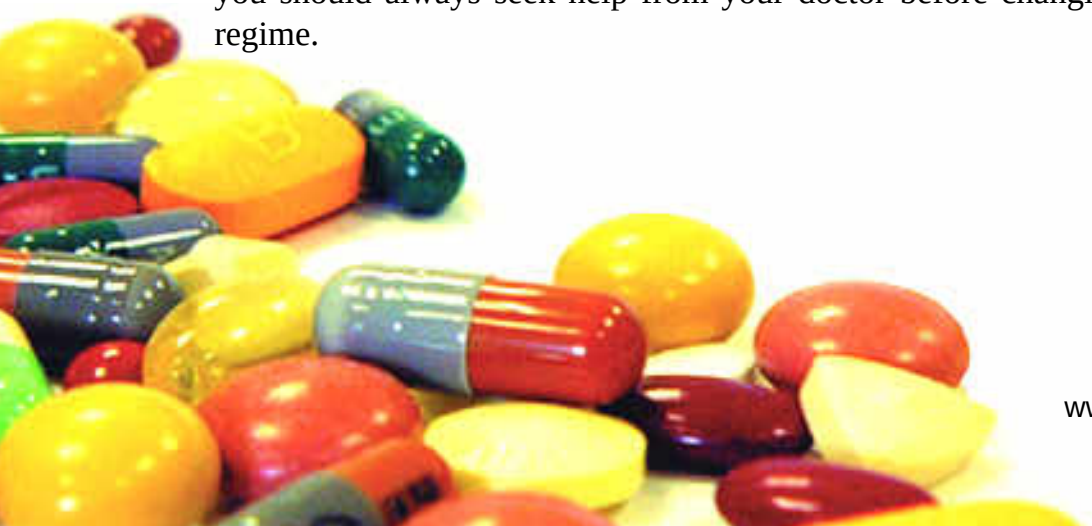
Side-effects

Drugs are generally licensed and tested to treat specific illnesses. What is referred to as side-effects is when the drugs affect the body in ways other than those that are intended. Most of the anti-HIV drugs have side-effects. It does not mean that everyone who takes them will experience side-effects. Generally, you cannot predict if you are likely to experience side-effects or not. Some people only experience the side-effects mildly and find them easily manageable. But for some people the side-effects occur so strongly that they have to consider other alternative drugs.

The most common side-effects are nausea and feeling tired. Side-effects are often referred to by the grade of the effect, and the grades range from mild to moderate to severe to life-threatening (based on the grading by the US NIH Division of AIDS). For example, it is considered a mild side-effect if a person has 2-3 vomiting episodes a day. Life-threatening side-effects such as extreme limitations in daily activity and hospitalisation are rare, but are still threats to some.

When drugs are developed they go through clinical trials. A clinical trial is a study with people to test how well the new drugs or treatment works and how safe it is. Some long-term side effects may not be noticed in the clinical trials. It is hard for the researchers to draw consistent information on side-effects in clinical trials, since people have different treatment histories, general health and tolerability levels. Therefore, some side-effects only become apparent after the drugs have been approved and have been used by more people over a longer period. Since HIV is a life-threatening disease, there is a constant need for new drugs. Sometimes it is important to get a drug on the market despite known side-effects. Many patients and health professionals agree that the anti-HIV drugs are far from perfect and the tolerability and side effects of the drugs need to be vastly improved.

It can be useful to find out about the possible side-effects that particular drugs have, before you start treatment. The side-effects often get better after you have been on the treatment for a while, as the body then starts to adjust to the anti-HIV drugs. Some people use alternative therapies and medications with the combination therapy to ease the side-effects. For example, some people find taking peppermint eases their feeling of nausea. Sometimes the side-effects do not diminish over time, and in some instances one or more of the drugs in the combination can be changed to reduce the side-effects. If you feel that the side-effects are too much to cope with, you should always seek help from your doctor before changing or stopping your regime.



Lipodystrophy

Lipodystrophy is the name given to changes which can occur in the way how fat is redistributes in the body. There are generally three ways in which the fact changes tend to take place:

1) Some people gain fat on the abdomen/stomach areas, between the shoulder blades, around the neck or in the breasts.

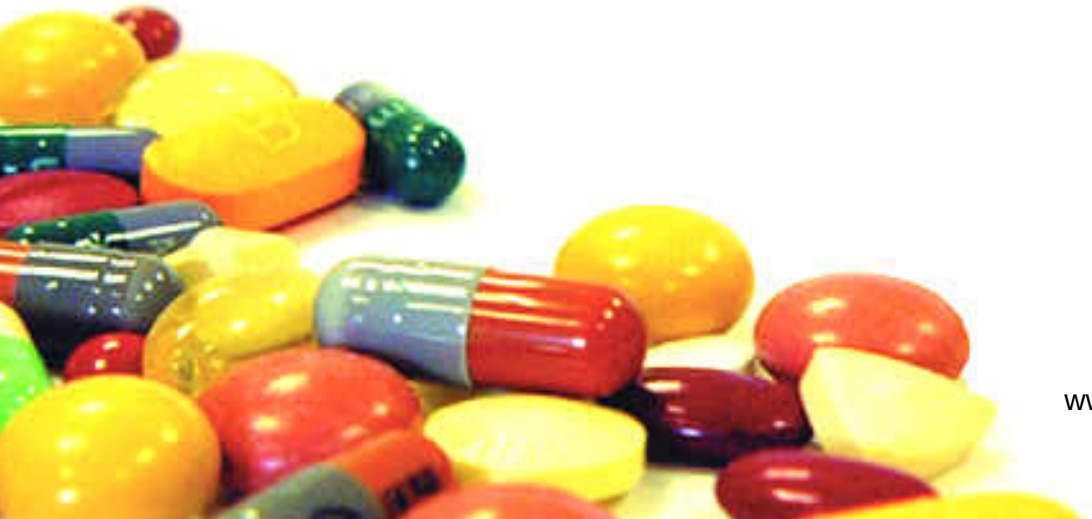
2) Some people loose fat from under the skin of their arms and legs, and they loose the shape in the buttocks. Some people experience fat loss that results in facial wasting or prominent veins in the arms and legs.

3) Some people experience lipodystrophy as mixture of both fat gain and fat loss.

The causes of lipodystrophy in people with HIV are still unknown. But lipodystrphy symptoms have been blamed on individual anti-HIV drugs, overall antiretroviral therapy or on HIV itself.

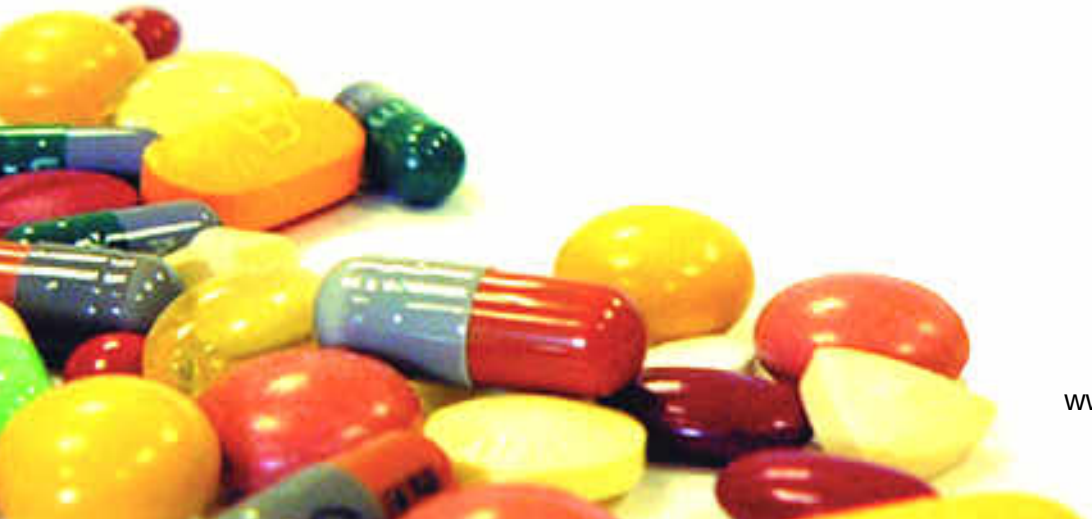
Although, the links between anti-HIV drugs, gender and lipodystrophy are not well known, some important findings have been made. Most of the research that has been done suggests that the longer you take combination therapy, the more likely you are to develop lipodystrophy. It has also been suggested that people who are taking protease inhibitors (PI) and nucleoside analogues (NRTI's) together seem to be more likely to develop changes associated with lipodystrophy than taking these drugs separately.

There is an on-going debate of which sex is more at risk of lipodystrophy. However, what seems clear is that women and men may be experiencing lipodystrophy differently. Weight gain and increases in breast size may be more common overall amongst women whereas men maybe more prone to suffer facial and limb wasting. Research is made hard with the difficulty of measuring lipodystrophy and it seems that weight gain is easier to measure that wasting.



The fact that the causes of lipodystrophy are still unknown makes it difficult to avoid and treat it. It was first though that lipodystrophy was caused by the protease inhibitors class of drugs, but then fat changes were seen in people who have never taken PIs. Often, the drugs that are the most successful at suppressing HIV and the best tolerated seem the most strongly linked to lipodystrophy. One explanation for this is that these drugs are usually used for longer. Alternatively, the new drugs are blamed for the problems that may have been started by previous therapy. Some researchers have reported that lipodystrophy may be caused by rapid and sustained decreases in viral load. So this would meant that lipodystrophy is not a problem with particular class of anti-HIV drugs but related to the potency of the total regimen. Lipodystrophy may also be caused by HIV itself interfering with how the body processes fats.

Lipodystrophy alone does not contribute to poor future health. However, body fat changes may cause some people feel embarrassed, uncomfortable and stigmatised. At the moment, all treatment for lipodystrophy are based on assumptions about what might be causing it and what can be done to prevent it. There is no evidence that choosing particular drug combinations, switching from one combination to another or stopping treatment reduces the risk of lipodystrophy. Some people have been using exercise and specific diet as the way to control body fat changes. There is little evidence to support this, but it can be helpful making people feel better. Some people feel that the changes have been so drastic that they go for the uncertain options of help such as facial surgery, hormones and steroids.



Adherence

The term adherence means taking the drugs exactly as prescribed. It also means taking the drugs on time and following any diet restrictions.

Adherence can seem difficult and sometimes there is a need to make changes to your lifestyle to adjust to the treatment. Developing a routine can help you to keep to your daily drug regime.

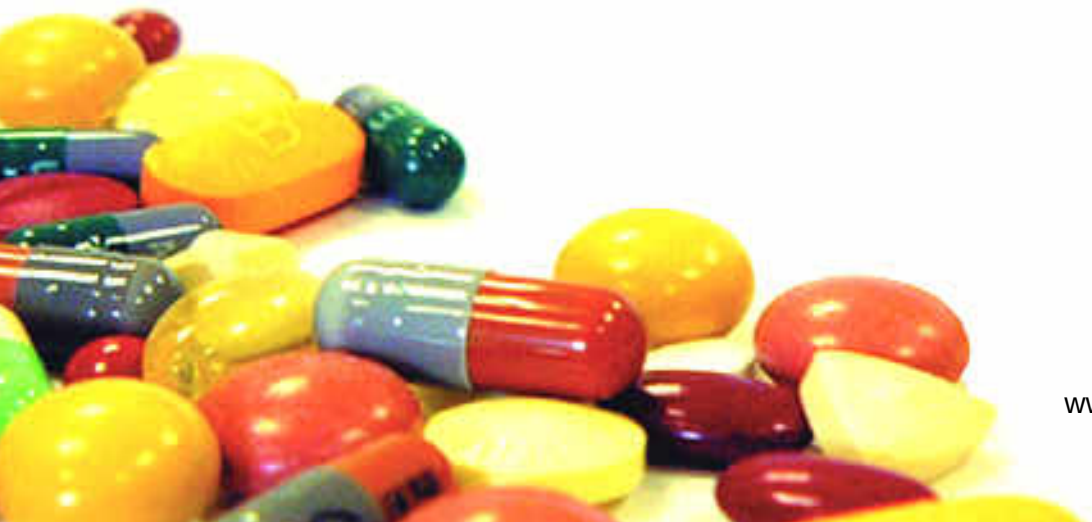
If you are starting combination therapy, it is important to concentrate on getting used to the drug regime. Give yourself some time and space to get it to work.

If the drug treatment instructions are not followed exactly, it is likely that the drugs will not be absorbed properly in the body. This will have serious short and long-term consequences. It will have an effect on the viral load. It is also likely that you may develop resistance to certain drugs. This will reduce the overall benefits you can get from the drugs in the future.

It is therefore important that you are committed to your treatment and try to make it as much a part of your lifestyle as you can.

Adherence and side-effects

Adherence is a very important part of anti-HIV treatment. Often experiencing side-effects makes adherence difficult. Your doctor might be able to give you some treatment to help with the most common side-effects such as nausea and diarrhoea. As adherence is such an important part of treatment, it is important to monitor closely the effect that side-effects have on your adherence. If the side-effects are affecting adherence, you must tell your doctor.



Starting Treatment

There is no proven 'right' time to start HIV treatment. The exact timing of starting your treatment should depend on individual factors such as symptoms, patient preference, likely adherence and possible toxicity. It is helpful to get some basic tests done to monitor the course of your HIV infection. Then your doctor can advise you about the timing of starting treatment. There are different views of the benefits of starting HIV treatment earlier or later. Either choice will have long-term effects and consequences. You also have to consider whether you are ready to start treatment or not. Commitment to the treatment is as important as the drugs themselves. Some people find it easy to make up their mind about treatment. For others, making a decision may take considerable time, and having many options may feel very confusing.

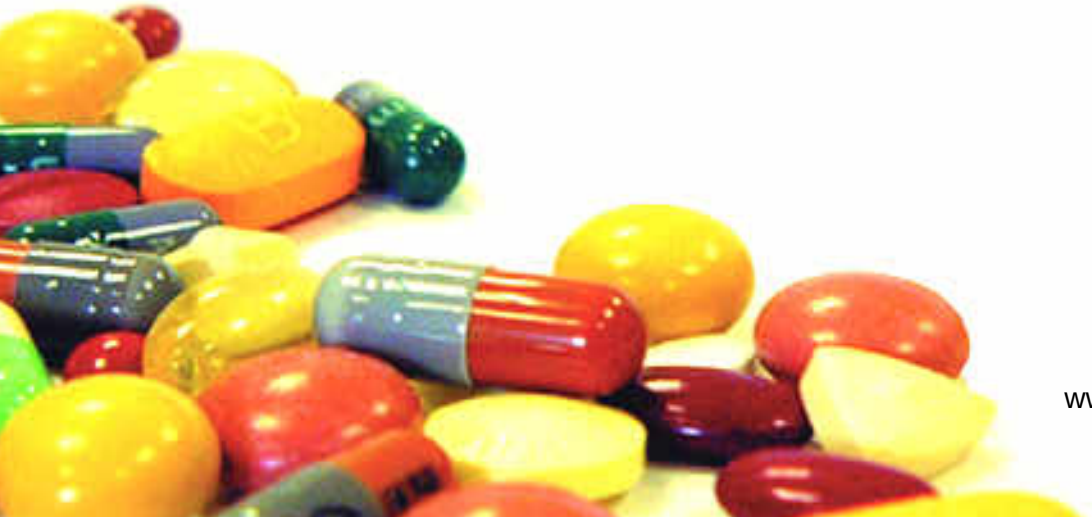
Deciding to Start

The viral load and the CD4 tests can help you to decide whether to start treatment or not. You should talk to your doctor about the results of the tests and what they indicate. The anti-HIV drugs should reduce the viral load to a level which is below the level of detection of the current tests, and the drugs should also boost the CD4 levels.

The general recommendation in the UK is to start treatment when the CD4 count is between 200 and 350 (details of the various guidelines about treatment are given in Appendix 3). It is strongly recommended to start HIV drug treatment when the CD4 count is above 200. A low CD4 count does not meant that you will certainly become ill, but it makes it more likely.

After considering the results of the tests, you can find out from your doctor about the various HIV drugs and combinations available, and which are suitable, including the positive and negative effects the drugs have.

You should start the treatment only when you are really ready. You need to be very committed, since following a drug regime can be quite demanding. Your commitment to the treatment is as important as the drugs themselves. Once the treatment is started, it is likely to be for life. So you should only start treatment when you feel that you can really be committed to it.



The Best Combination

For most people there are a number of drug combinations available that might work, as there are now 4 different groups of antiretrovirals and 20* fully approved individual drugs. Your doctor should be able to suggest the best combination for your CD4 count and viral load. It is hard to tell which is the best combination, since a combination that suits one person might not suit another.

It is important that the combination of drugs works medically. What is also important is that the drugs can be taken well and on time. It is essential to consider the restrictions and limitations that the drugs may have on your lifestyle.

These are some of the issues that need to be considered:

- How many pills are there, and how many times a day do they have to be taken?
- Are there any food restrictions?
- What are the possible side-effects?
- Are there other drugs or complimentary therapies that cannot be used?
- What is the size of the pills?
- Are there any special handling requirements?

Usually the drugs must be taken twice or three times a day, depending on the combination, although there are starting to be more combinations that only need to be taken once a day. Some of the drugs have food restrictions, which have to be followed carefully.

Some anti-HIV drugs have known side effects. The side-effects can have a considerable effect on every day living and activities. Also, the size of some of the larger drugs can be a problem. Some antiretroviral drugs also require special handling, such as refrigeration, and for some people this may cause problems. For some people dealing with many drugs is not easy. There are some combination drugs available that have 2-3 antiretrovirals in one capsule to ease off the ‘pill burden’.

The first time you use antiretrovirals is the time they will be the most effective. This is why you should try to get the combination right the first time.

*UK March 2004

Drug Interactions

When taking more than one antiretroviral drug, the drugs can sometimes react with each other, or with certain food, other medication or herbal remedies. This is called drug interaction.

Drug interactions occur when the antiretroviral are absorbed, broken down and removed from the body through a range of reactions and processes. This happens in different parts of the body, for example, in the stomach, kidneys and liver. Drug interactions can occur straight away after starting the treatment or develop over period of time. Drug interactions often cause changes in the drug levels in the body. The change in drug levels can lead to drug failure or side-effects.

The interaction between antiretroviral drugs can cause changes in the effectiveness of one or more of the drugs. The effectiveness of the drugs can increase or decrease.

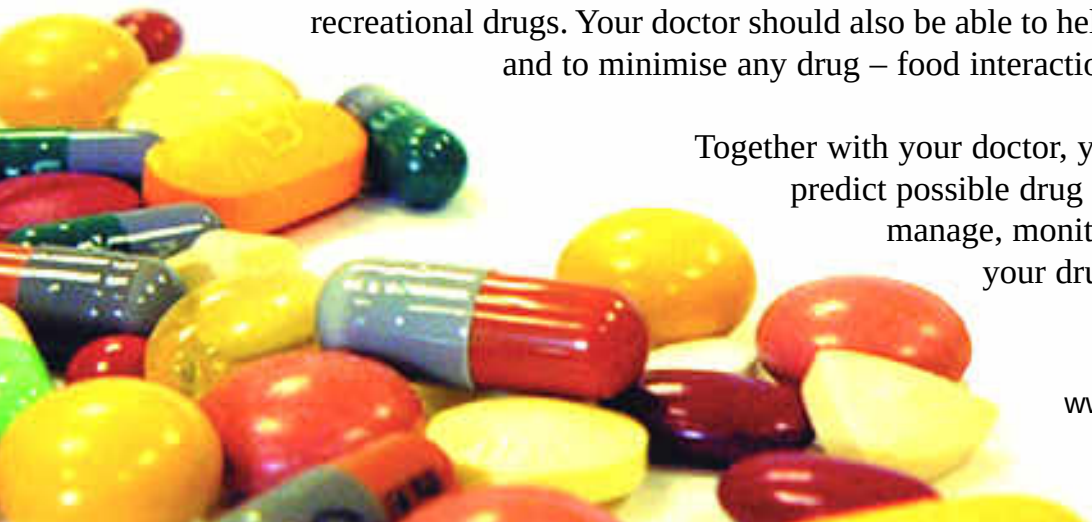
The drugs can interact and cause drug levels to drop in the body. If this happens, there is a potential threat of drug resistance or illness occuring. When there is not enough antiretroviral drug in the body, the virus is able to start to reproduce itself. This will increase the risk of getting ill. Also, when the virus is not fully suppressed, the more chance the virus has to develop resistance to the anti-HIV drugs.

Alternatively, the drug interactions can sometimes trigger off an increase in drug levels in the body. When the drugs react with each other or something else, the level of effectiveness increases over the level needed. Often, the body is not able to cope with the increased drug levels and you may experience strong, in some cases even life-threatening side-effects.

Some drugs simply should not be taken together while some can be used with careful monitoring. The research into drug interactions has been narrow and has mainly evaluated the effect of one drug on another. What makes drug interactions difficult to study is that each individual is different and reacts to drugs differently. Also, the range of medication and multidrug combinations make drug interactions hard to predict and generalise.

There can also be interactions between anti HIV drugs and other drugs you may be taking. So you should ask your doctor's advice if you are taking or thinking of taking any other medication; prescription or non-prescription, herbal remedies or recreational drugs. Your doctor should also be able to help you with your diet and to minimise any drug – food interactions.

Together with your doctor, you should be able to predict possible drug interactions and manage, monitor and even adjust your drug regime.



Mother to Child Transmission & Pregnancy

Mother to Child Transmission (MTCT)

Antiretroviral drugs are one of the number of interventions that can be used to help prevent HIV being passed from a mother to her unborn child.

Mother –to-child transmission (MTCT) also known as vertical transmission may occur

*Before birth
*During birth
*After birth through breastfeeding

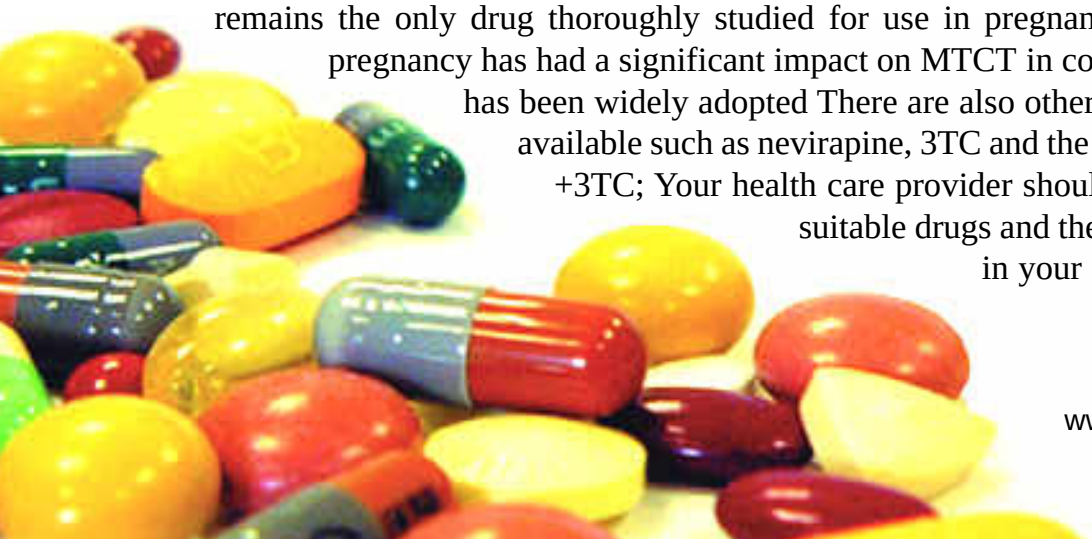
A woman can minimise the risk of HIV being passed to her child by certain interventions. These include:

- taking antiretrovirals during pregnancy (excluding the first 3-4 months of pregnancy),
- taking antiretroviral drugs during labour
- choosing caesarean section as the method of delivery
- giving the baby a short course of antiretroviral therapy after birth
- abstaining from breast-feeding

In many countries women take advantage of all of the available interventions and this has resulted in a very low transmission rate of HIV from mother to child. With no interventions the rate of transmission can be in the region of 25-45%. With all interventions the rate can be as low as 2% In countries where fewer facilities are available, there has been some success in reducing the transmission rate by use of a small dose of drugs during labour.

Generally, the antiretroviral drugs will not be recommended for the mother before weeks 12- 14 of pregnancy, unless there is an urgent medical reason. The main reason to wait is that the antiretroviral drugs could have an adverse effect on the baby in the early stages of it's development.

The first drug that was used to prevent MTCT of HIV was AZT in 1994. AZT remains the only drug thoroughly studied for use in pregnancy. AZT use during pregnancy has had a significant impact on MTCT in countries where its use has been widely adopted There are also other alternative drugs available such as nevirapine, 3TC and the combination of AZT +3TC; Your health care provider should have details about suitable drugs and the availability of them in your country.



One widely used option for HIV-positive women is to take antiretroviral drugs during labour. Antiretroviral drugs taken during labour can minimilise the risk of transmitting HIV from mother to baby and in some countries with fewer facilities, this is the only way available to prevent mother to child transmission of HIV. In many countries, which lack medical facilities, small doses of nevirapine are provided during labour free of charge by the manufacturer.

There is no firm recommendation of the‘safest’ route of delivery of the baby when you are HIV-positive. The two ways of delivering your baby, vaginal delivery and caesarean (c-section) both have their benefits and risks. Caesarean section is an operation used to deliver a baby through its mother’s abdominal wall. With HIV-positive mothers, caesarean sections are increasingly planned and performed before the onset of labour to protect the baby from direct contact with the mother’s blood and genital tract secretions. This procedure is called elective caesarean section. To further minimise the baby’s contact with the mother’s blood, a ‘bloodless caesarean section’ use is being advocated. This method of delivery involves controlling the mother’s blood vessels (by heat, cold, electricity or staples) so the bleeding is blocked.

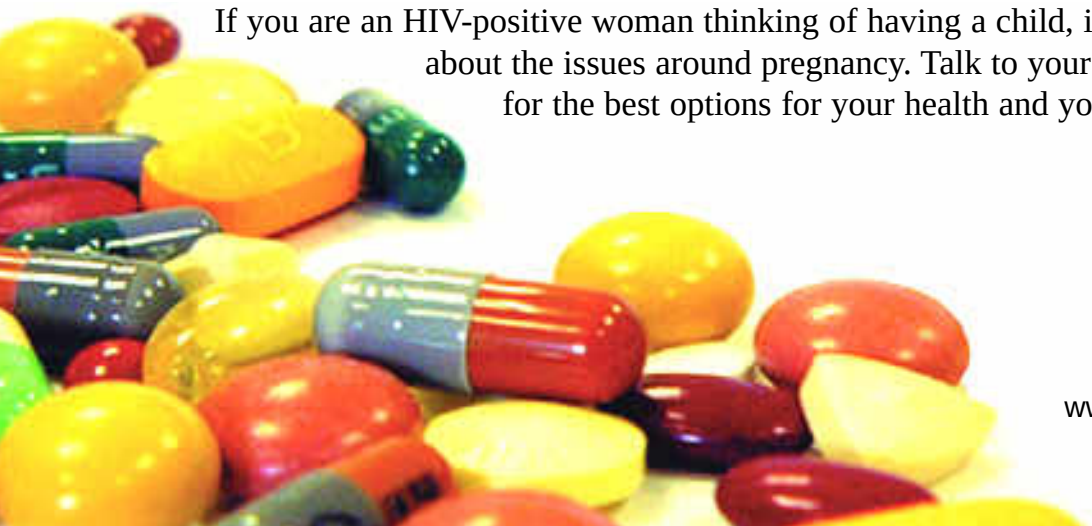
For women who have an access to good prenatal care and HAART it is not know whether caesarean section provides any additional benefit to the use of effective HAART. Although, the benefits of caesarean may sound appealing some doctors will not recommend it because of the risks to the mother’s health In resource-limited countries caesarean section may pose a risk of infection or may simply be unavailable.

In countries where antiretrovirals are available, it is standard prevention practice to give anti-HIV drugs to infants born to HIV-positive women for a certain period of time.

HIV is found in breast milk. Women with HIV are, therefore, advised not to breafeed when they have access to safe milk substitutes. Without any other interventions, the overall rate of mother-to-child –transmission of HIV is about 15-25% among HIV-positive women who do not breastfeed and 25-45% among HIV-positive women who breastfeed.

Becoming pregnant if you are HIV-positive

If you are an HIV-positive woman thinking of having a child, it is good to think about the issues around pregnancy. Talk to your health care provider for the best options for your health and your baby’s health.



You may feel that you baby's health is the most important thing, but remem ber you health is as important. You should receive the same standard of care that is available to any woman who is thinking of getting pregnant or is already pregnant.

Positive women who are pregnant are as healthy as those positive women who are not pregnant. An HIV positive woman who is pregnant, can consider taking anti-HIV drugs to help her own health, as well as taking them to prevent mother to child transmission of HIV. In certain countries, HIV positive women have the opportunity to consider taking drugs during labour, choose the method of delivery, abstain from breastfeeding and give their babies certain anti-HIV drugs. These intervention methods are explained in more detail above.

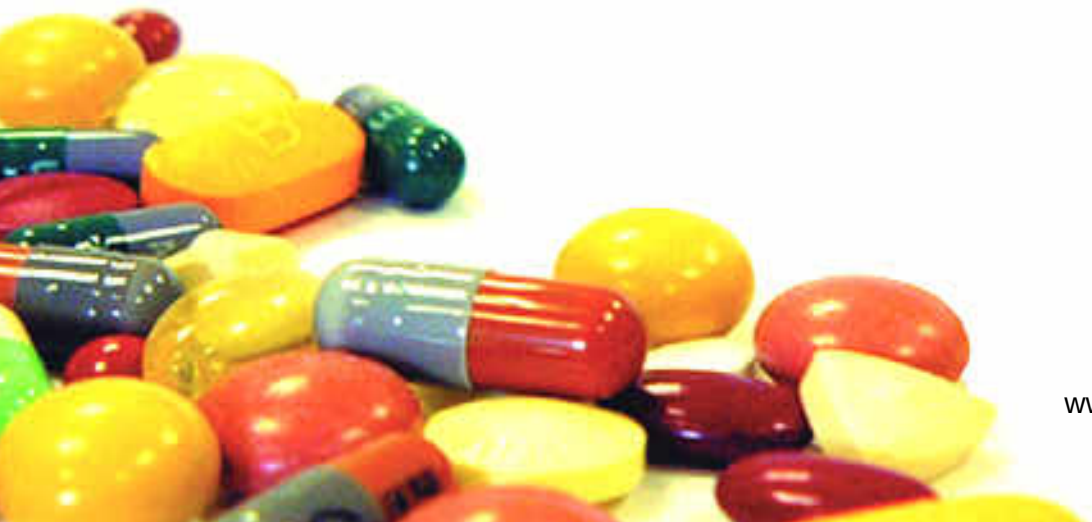
Sometimes an HIV positive woman who is already on treatment will find out that she is pregnant. Advice should be obtained urgently from your doctor about what it is best for you to do. It may be sensible for the you to change the drugs that you are taking, as some drugs are more suitable during pregnancy than others. It is not a good idea to come off or change your therapy before seeing your doctor. If the treatment is stopped and the viral load rebounds, there may be an increased risk of HIV transmission to the baby. If you are thinking of changing or stopping your treatment, you must see your doctor.

Learning you are positive when you are pregnant

Sometimes a woman will find out that she is positive when pregnant. Obviously, a major concern is the well being of the child, but as explained above there are certain things that can be done to prevent HIV being passed on from the mother to the child. In many countries there are antiretroviral drugs and other interventions available that can help to prevent your baby getting infected, as well as, to maintain your health. It is important that you talk to your health care provider about the best options available to you and your baby.

Testing

Your baby can have an HIV test but it will not necessarily show straight away whether the baby is infected. All babies born to mothers with HIV are born with HIV antibodies. Babies who are not infected lose their antibodies by the time they are around 18 months old.



Changing Treatment

The goal of anti-HIV treatment is to stop you from becoming ill for many years. Sometimes the antiretroviral therapy works without any major problems or setbacks, but sometimes there can be problems. The antiretroviral drugs have not been available for that long, and despite on-going research and development, there are certain problems, which can occur.

There are two main reasons why anti-HIV treatment sometimes needs to be changed.

Firstly, a change of treatment is needed when the antiretrovirals fail to work and slow down the reproduction of the virus in the body. Increased viral load or an HIV-related illness are signs of failing anti-HIV treatment.

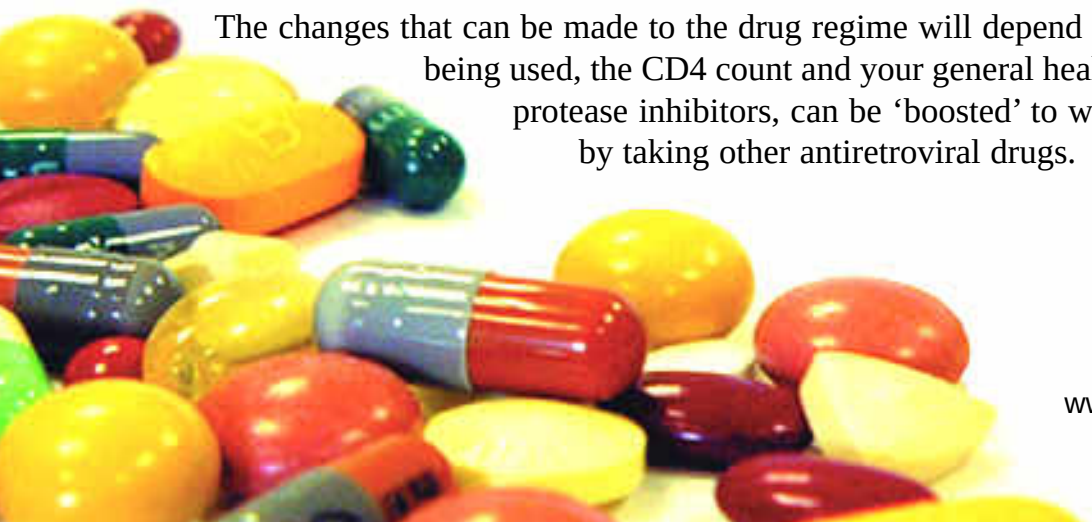
There are a number of reasons why the antiretrovirals may not be working. These include:

- the combination of drugs was not strong enough
- the drugs were not being absorbed in the body properly
- resistance has developed to the drugs
- poor adherence.

Also, the drug combinations often cause side-effects, and sometimes these side-effects are so strong, intolerable and even life-threatening that the treatment must be changed.

Monitoring the viral load carefully is an important part of treatment. But there are different opinions about the 'right time' to change the treatment if your viral load is rising. Some doctors recommend changing the treatment as soon as the viral load starts to rise. Others recommend monitoring the overall trend of the viral load before making a decision to change. Changing the drugs earlier rather than later, could mean running out of treatment options quicker. But changing later, means there is a danger of developing resistance to certain drugs. This can seriously limit your future treatment options.

The changes that can be made to the drug regime will depend on the drugs already being used, the CD4 count and your general health. Some drugs, like protease inhibitors, can be 'boosted' to work more effectively by taking other antiretroviral drugs.



The ‘boosting’ of protease inhibitors can sometimes be option to increase the drug levels in the blood and changing treatment will not be necessary.

The changes that need to be made also need to take into account the reason for the reatment failing. For example, if resistance has developed, this may be because of poor adherence, and a simpler regime that is easier to adhere to may be needed.

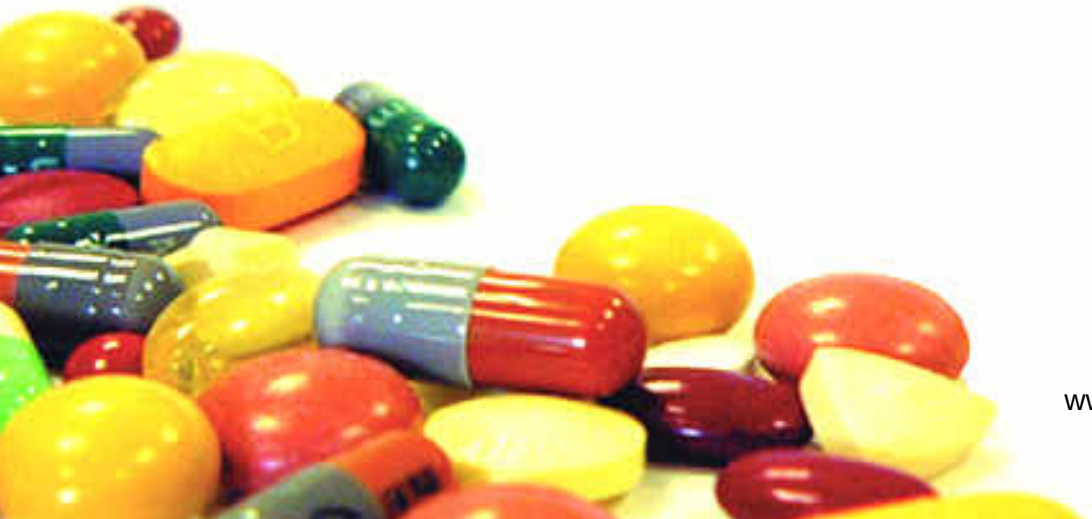
The anti-HIV drugs work the best when used the first time. This is one of the reasons why it has to be considered carefully whether a change of treatment is necessary or not. The combination of anti-HIV drugs other than the first or second treatment is called salvage therapy. It is also referred as second-line, third-line or rescue therapy.

Many people start their salvage therapy with much higher levels of viral load than previous treatments. This puts more pressure on the new combination to work. Each combination used lessens the chance of maintaining a low viral load because of the possibility of developing resistance to the drugs. The choice of new treatment should always depend on what caused the previous one to fail.

If you have an increased viral load, strong side-effects or need to change your anti-HIV treatment for any other reasons - always contact your doctor before taking any action.

Structured Treatment Interruptions (STIs)

Structured Treatment Interruptions (STIs) or drug holidays are the terms used when someone is stopping taking anti-HIV treatment for a certain period of time. People take treatment interruptions for a variety of reasons, such as side-effects, ineffectiveness of the drugs and psychological matters. STI does not mean skipping or stopping your medication randomly, but taking a break from your drug regime with a planned timescale, close monitoring and help from your doctor.



In theory, STIs have benefits such as stimulating the immune system, reducing side-effects and lowering the cost of medication. Enjoying a drug-free period is also believed to have some psychological benefits such as increased adherence when returning to treatment. If the immune system responds well to the STI, it often means there is the possibility of a longer drug-free period. However, after a period without anti-HIV drugs, most people have to start their treatment again. Some studies have found that people who were resistant to certain antiretrovirals were less resistant to the same drugs after a treatment break.

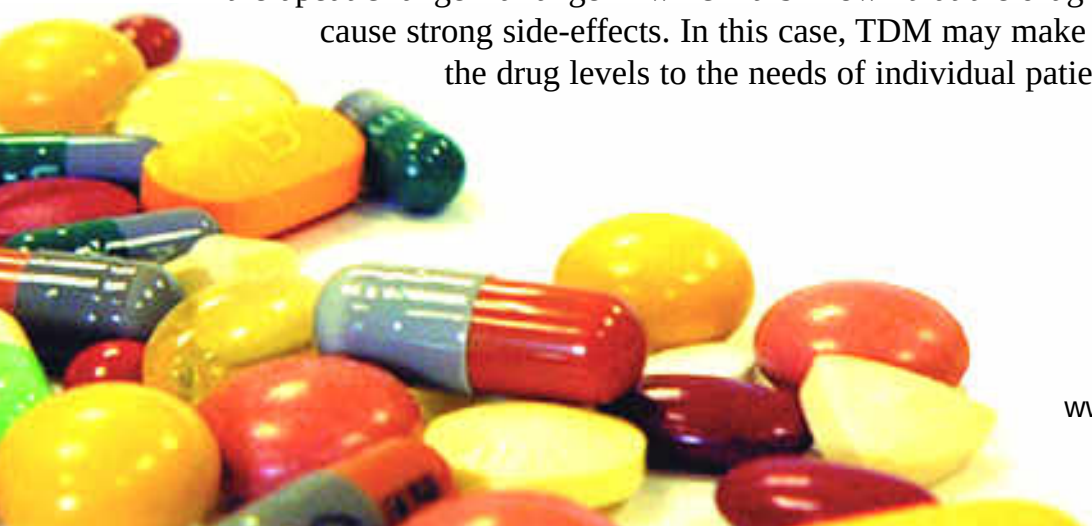
The main risks of using a treatment break are that the viral load will rise and the CD4 count will drop. This may increase the risk of becoming ill. Also, stopping and re-starting the treatment could make it easier for the virus to develop resistance to the anti-HIV drugs.

Some research has been carried out about the benefits and risks of interrupting anti-HIV treatments. However, long-term effects are unknown. STIs are not widely recommended for general use at the present. If you are considering treatment interruption or stopping your treatment - always talk to your doctor first. Taking unsupervised treatment breaks can do more harm than good to your health and limit you treatment options in the future.

Therapeutic Drug Monitoring (TDM)

Therapeutic drug monitoring (TDM) means measuring the amount of a particular anti-HIV drug from a blood sample. It is important that the drug levels in the body are adequate, so the antiretroviral therapy can work properly. Too little drug in the body and HIV is able to reproduce itself again. Too much drug can mean experiencing strong side effects. TDM can offer help to some people in understanding how their bodies cope with certain drugs.

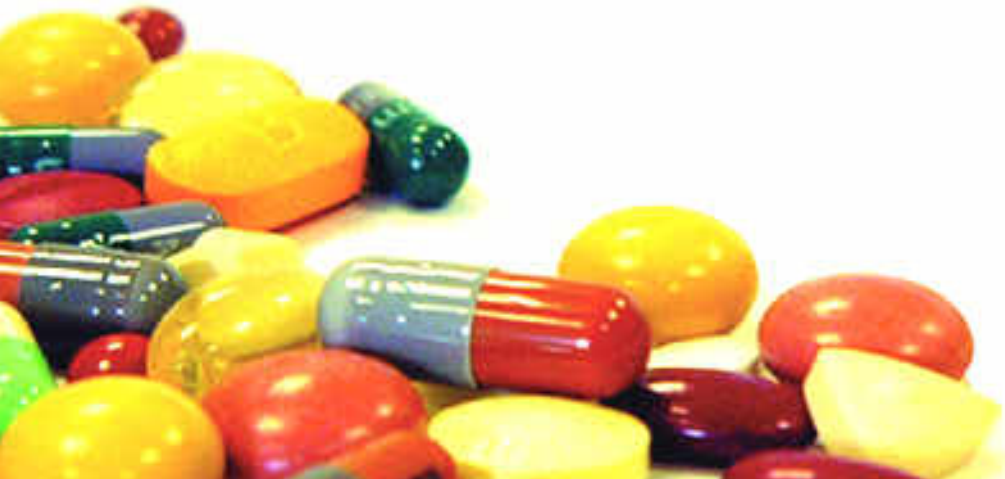
Many things affect how the antiretroviral drugs are absorbed in the body. Food intake, weight, age, hepatitis C, and liver/kidney dysfunction can have an effect on how the body 'deals' with the drugs. Different people have a different pattern as to how the drug is both absorbed and eliminated from the body. In particular, it is known that the levels of protease inhibitors can vary a great deal between individuals. TDM may be used for ensuring that the levels of the drugs are in the 'therapeutic range'- a range in which it is known that the drug works and does not cause strong side-effects. In this case, TDM may make it possible to adjust the drug levels to the needs of individual patients.



There are particular difficulties with certain drugs. For example, using TDM to test the levels of nucleoside analogues (NRTI) is difficult. NRTI's are processed inside individual cells before they work against HIV. The level of NRTI inside the cell is much more important than the amount in the blood. Testing the level inside a cell is much more difficult than drug monitoring of the blood. This makes hard to predict what effect the NRTI drug levels have on side-effects and how the drug works overall.

Some researches believe that TDM can help to get the drug levels right and that it benefits a range of people. For example in situations when people are suffering from high-levels of side-effects or when treatments fail despite adherence. But some researchers are critical of therapeutic drug monitoring and it is not available in many countries.

Another difficult factor with TDM is that there is not just one target level for each drug. The target level of the drug depends on how resistant the virus is to the drug. The more resistant the drug, the higher the level of the drug needed to control it.



Appendix 1

Sources of Further Help and Advice:

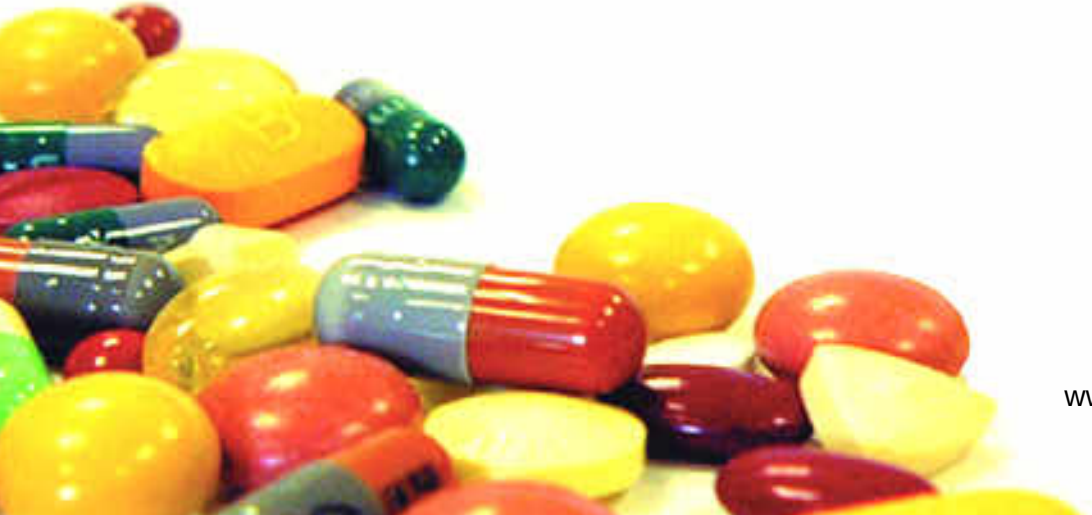
Websites:

- HIV i-Base www.i-base.info
- AIDS Meds www.aidsmeds.com
- Project Inform www.projectinform.org
- Medline Plus
  www.nlm.nih.gov/medlineplus/aids.html
- AIDS map www.aidsmap.com
- The Body www.thebody.com/treatment.html
- HIV in Site http://hivinsite.ucsf.edu/InSite

Helplines:

In the UK:

- The HIV I-Base treatment information phone line
  (Mon, Tues, Wed 12-4pm)
  0808 800 6013
- Living well with HIV phone line
  (Mon-Thu 6 pm – 9 pm)
  0845 947 0047



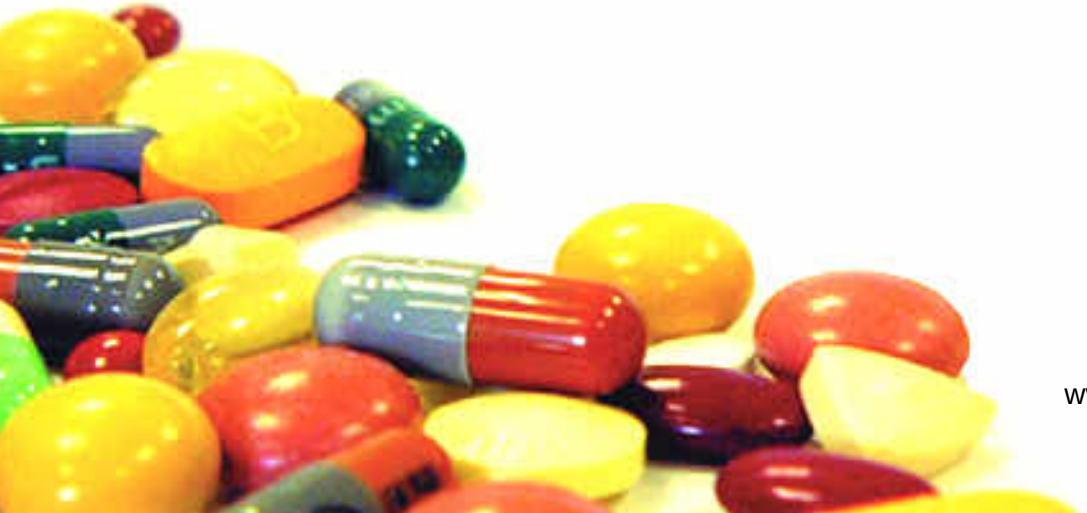
In the U.S:

- The Project Inform National HIV/AIDS treatment hotline
  (Mon – Fri 9 am – 5 pm, Sat 10 am – 4 pm [Pacific Time])
  1-800-822-7422 (toll-free in the U.S.) or 415-558-9051 in San Francisco Bay area or internationally
  International 1-415-558-9051

- AIDS Treatment Data Network
  U.S. 800- 734-7104
  International 212-260-8868
  (Mon - Fri 9 - 6 [Eastern Time])

- AIDS INFO
  (Mon-Fri 12 pm – 5 pm [Eastern Time])
  U.S. 1-800-448-0440
  International 1-301-519-0459
  Fax: 1-301-519-6616

Other international helplines and organisations can be found at http://www.thebody.com/hotlines/internat.html



Appendix 2

Basic Information about HIV & AIDS

What is HIV?

HIV stands for the Human Immuno-deficiency Virus. This is a virus that people can become infected with and that they can then pass on to other people.

How is a person affected by HIV infection and when does it become AIDS?

When someone becomes infected with HIV it begins to attack their immune system which is the body's defence against illness. This process is not visible.

A person infected with HIV may look and feel perfectly well for many years and they may not know that they are infected. Then as the person's immune system weakens they become vulnerable to illnesses, many of which they would normally fight off.

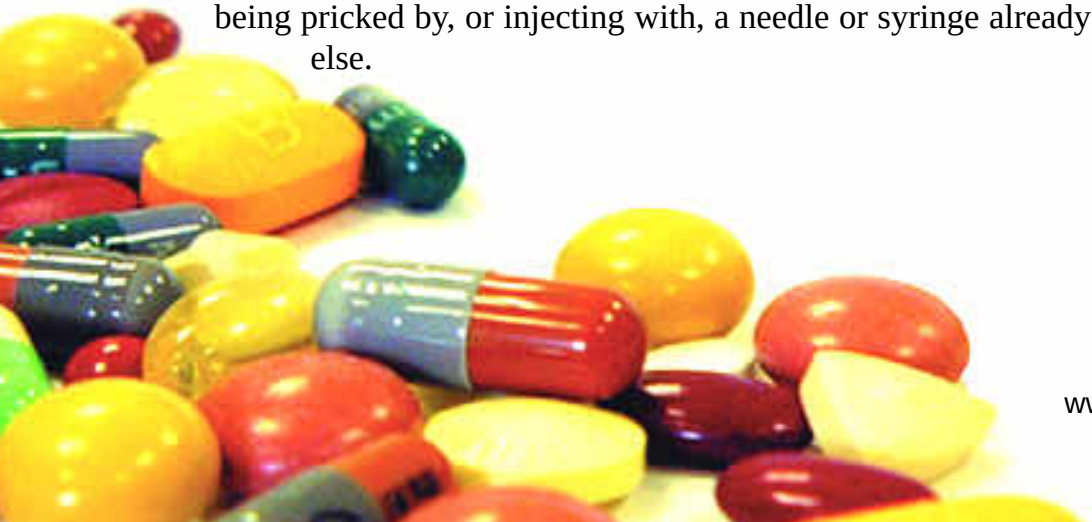
When a person is infected with HIV they are likely as time goes by to be ill more and more often. A person is said to have AIDS (Acquired Immune Deficiency Syndrome) when, usually several years after first becoming infected with HIV, they have developed one of a number of particularly severe illnesses.

How exactly is HIV passed on? What is a 'risky activity'?

HIV is present in the sexual fluids and blood of infected people. It can also be in the breastmilk of infected women.

A risky activity is anything that makes it possible for the virus to pass from one person to another. This is why sexual intercourse without a condom is risky, because the virus, which is present in an infected person's sexual fluids, can pass directly into the body of their partner. Using a condom properly is a very effective way of preventing transmission of HIV during sexual intercourse.

Contact with an infected person's blood is risky if it allows the virus to pass into another person's body through cuts or grazes in their skin. This is why it can be risky being pricked by, or injecting with, a needle or syringe already used by someone else.



It is also possible for an infected woman to pass the virus on to her unborn baby either before or during birth. HIV can also be passed on through breast-feeding.
It is not possible to become infected with HIV through:

* sharing crockery and cutlery
* insect/animal bites
* touching, hugging or shaking hands
* eating food prepared by someone with HIV.

What is Safe Sex?

Safe sex refers to sexual activities which do not involve any sexual fluid from one person getting into another person's body. If two people are having safe sex then even if one person is infected there is no possibility of the other person becoming infected.

Safe sex activities include hugging, touching, caressing and mutual masturbation.

What about kissing? Can you become infected by kissing someone who has HIV?

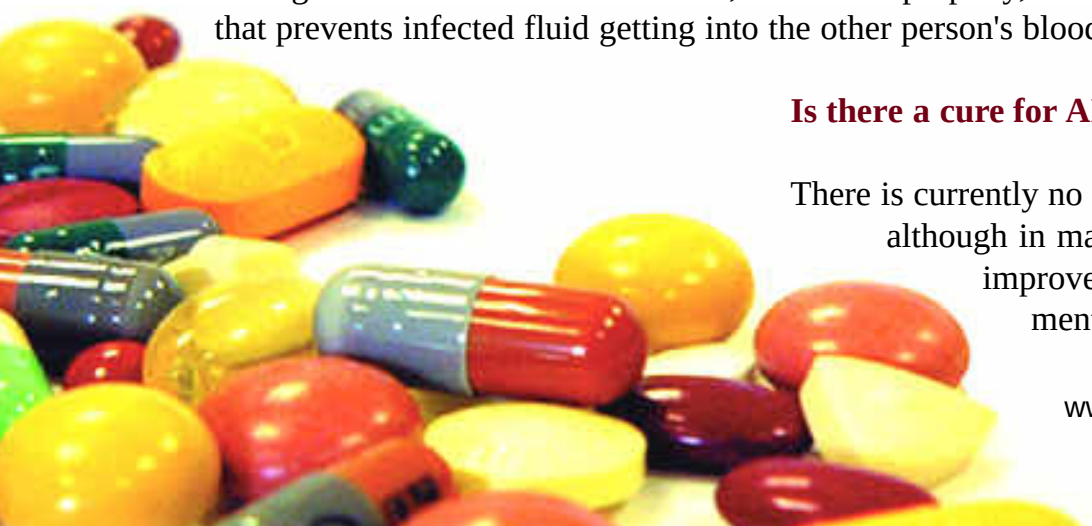
Kissing someone on the cheek, also known as social kissing, does not pose any risk of HIV transmission. Deep or open mouthed kissing is considered a very low risk activity for transmission of HIV. This is because HIV is present in saliva but only in very minute quantities, insufficient to lead to HIV infection alone.

There has only been one instance of HIV infection as a result of kissing. This was as a result of infected blood getting into the mouth of the other person during open mouthed kissing. If you or your partner have blood in your mouth, you should avoid kissing until the bleeding stops.

What is safer sex?

Safer sex is used to refer to a range of sexual activities that hold little risk of HIV infection or other sexually transmitted diseases.

Safer sex is often taken to mean using a condom for sexual intercourse. Using a condom makes it very hard for the virus to pass between people when they are having sexual intercourse. A condom, when used properly, acts as a physical barrier that prevents infected fluid getting into the other person's bloodstream.



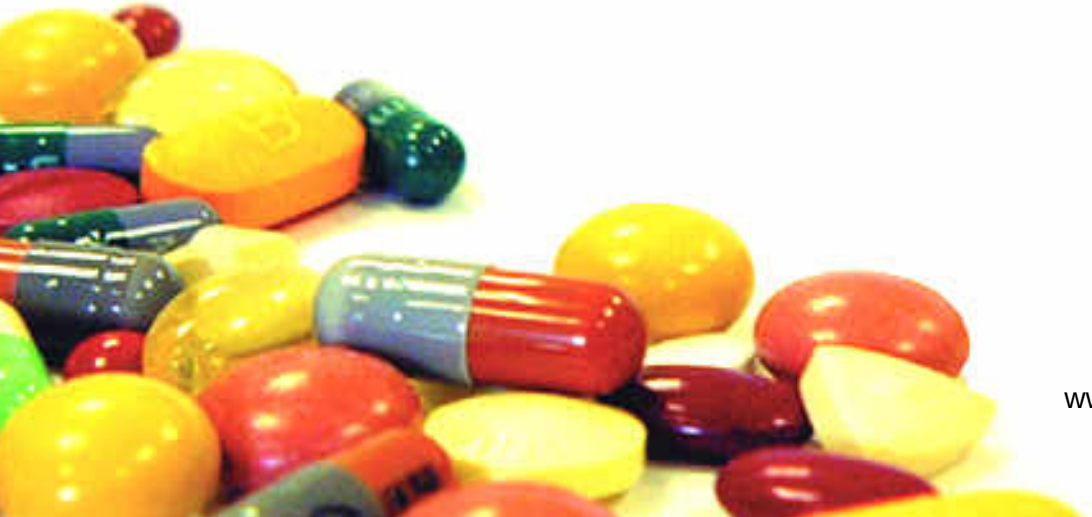
Is there a cure for AIDS?

There is currently no cure for AIDS although in many countries greatly improved medical treat ments are now available.

Appendix 3

Treatment Guidelines:

- British HIV Association http://www.bhiva.org/guidelines.htm
- CDC http://www.cdc.gov/hiv/pubs/guidelines.htm
- WHO : Guidelines for Antiretroviral Therapy in Resource-Limited Settings
  http://www.who.int
- Guidelines for the management of HIV infection in pregnant women and the prevention of mother-to-child transmission by British HIV association http://www.bhiva.org/guidelines.htm



Appendix 4

Clinical Trials:

A clinical trial is a study with people to find out how well a new drug or treatment works and how safe it is. Clinical trials are carefully planned medical experiments. They are normally managed by a hospital or health centre on behalf of the drug companies.

Clinical trials normally test entirely new drugs, a combination of existing drugs, or adding a new drug to old combinations. Also, clinical trials are used to evaluate new ways of dosing the drugs, for example, three times a day as an alternative to twice a day. Trials can help researchers to see how a new drug behaves in combination with existing drugs and also how beneficial a drug is compared to the current standard treatment.

Every clinical trial must have a plan called a protocol. The protocol determines, for example, who can take part, the timetable of the study, the length of study and how the treatment will be given. The protocol must be approved by an ethics committee. An ethics committee is made up of people who are separate from the people who are financing and running the trial. This is to protect the rights of the participants.

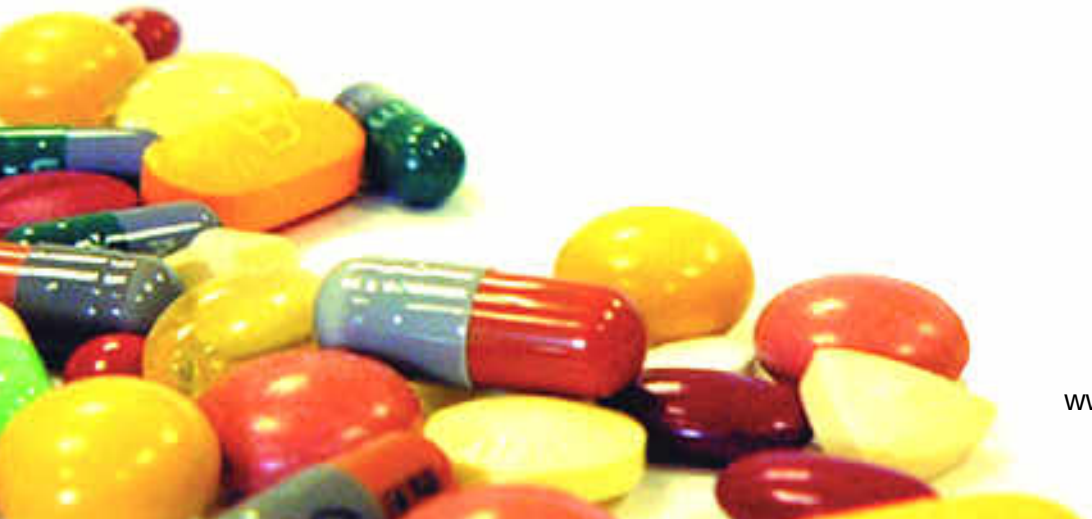
The Phases of Clinical Trials

Clinical trials normally consist of three or four stages or phases.

In phase I only a few people will test the medicine, and this will normally be people who are not HIV positive and who are not on any other medication. This phase tests the basic safety of a drug in humans.

In phase II the goal is to determine the correct dose of the new drug and assess whether the treatment is working in the short term.

It is only in Phase III that the effectiveness of a drug starts to be determined. In phase III there will be a very much larger group of participants. The time scale of a clinical trial varies from phase to phase, with phase III normally lasting at least 12 months.



Joining a Clinical Trial

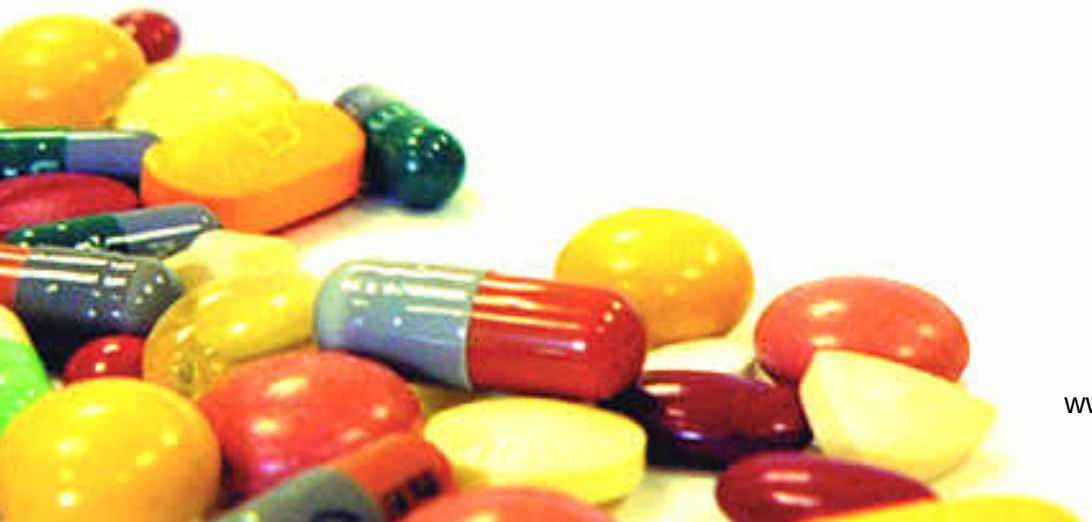
Each clinical trial has its own rules and criteria of who can join in. Sometimes the protocol excludes certain groups of people from participating in the clinical trial. The reasons to exclude people from a trial often include health reasons, such as interaction with existing treatment, pregnancy and a similarity of existing treatment to the one being tested.

Different people have different reasons why they night join or not join a clinical trial. It is your choice and you should never feel pressured to join, if you do not want to. If you refusing to join a clinical trail, you will still have exactly the same rights to medical care than anyone else.

For some people one of the most important reasons to join a clinical trail is to get access to new drugs. The clinical trials can offer a valuable chance if you have run out of treatment options due to resistance or side-effects. Some people also feel that one benefit of being in a clinical trial is the frequent monitoring and access to more advantaged tests as well as helping other people by participating.

There are also reasons for not joining a clinical trail. If you are on treatment that works well without many complications, joining a clinical trial is not usually recommended. There is a risk that the new treatment will not work as well as your current combination. This may harm your health more than benefit it. Also, most trials exclude women who are pregnant or wanting to get pregnant because of the unknown effects that the drugs may have on the unborn child. Another reason for not joining a trial is that it is likely to increase the visits you need to make to hospital and you may experiencing more rather than fewer side-effects.

There is no set or right time to join a clinical trail. If you are thinking of joining a clinical trial, seeking information and independent advice can be helpful as well as consulting your doctor. The only time when joining a clinical trial is specifically recommended is when there are no more treatment options available among the currently approved drugs. Then, the experimental drugs may be your best chance for staying healthy.



Types of Trial

Comparison Trial

A comparison trial is the most common type of clinical trail. This type of trial compares a group of people who are receiving the new treatment to people who are receiving the current standard treatment. Normally people who are receiving the new drug also receive their standard therapy.

Placebo- Controlled Trial:

A placebo is a pill or a drug that has no medicine in it, but which looks and tastes like a pill that contains a drug. In some clinical trials, different groups of people are given either a new drug or a placebo to be taken with their existing treatment. The participants of the trial do not know who is receiving the new drug and who is receiving the placebo.

Other Terminology

Randomisation

When people join a clinical trial they are put into different treatment groups at random. This should ensure that the people taking different drugs, or different combinations, are broadly similar. This makes comparing the results of the different treatment groups easier.

Blinded studies

A clinical trial or study is called ‘double-blind’ if neither the researchers or the participants know who is in a particular treatment group. I.e. As the trial is taking place they do not know who is receiving the new treatment and who is in the other group.

A clinical trial is a single-blinded study if only the researchers know which of the participants are receiving the new treatment.

Some clinical trials are ‘blinded’ to prevent people’s expectations from affecting the results of the trial. The researcher may unconsciously assess the participant differently and the participant may describe symptoms or side-effects differently if the treatment is known.