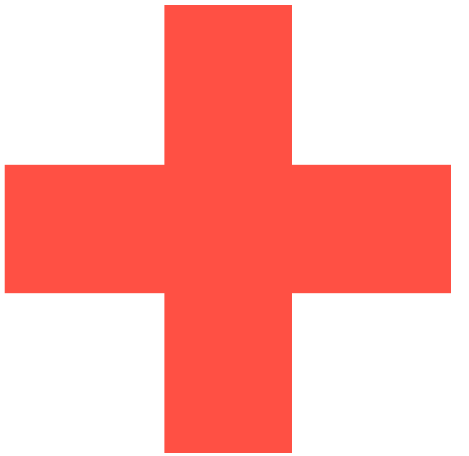
Opportunistic infections and conditions in the antiviral age

Q&A



Opportunistic infections and conditions in the antiviral age

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Introduction

This is a book about the opportunistic infections sometimes associated with HIV and AIDS. Combination antiviral treatments have dramatically reduced the number of people with HIV who progress to AIDS-related illnesses or infections. Many of these infections are now infrequently or rarely seen by HIV GPs and specialists. However, people with HIV, even those on combination therapy, are still at risk of these illnesses, especially if you have a low CD4 count. This booklet looks at some of these illnesses and conditions, and provides information about how to prevent, manage or treat them. This booklet does not deal with the long-term side effects or toxicities associated with anti-HIV treatments. This is a separate and complex issue, and is dealt with more thoroughly in a number of resources, in particular, the *SOS Drug Guide.*

How should it be used?

This booklet is meant to provide information, and should be used in consultation with your healthcare providers. It is not intended to be, and shouldn't be used as, a definitive 'manual' on what is an enormously complicated area. There are conditions which we have not included in here, and treatments and care standards can and do change. It's really important that this book is not used as a 'how to' for the management or treatment of any of the conditions described. If you think you are at risk or could have one of these or other conditions, you should seek advice from your GP or referral to a specialist.

What are opportunistic illnesses?

The term opportunistic illnesses (OIs) refers to a number of illnesses, infections and conditions which occur in people whose immune systems have been damaged due to HIV and AIDS. They can also occur where people's immune systems are damaged due to auto-immune conditions, cancer, or some immunosuppressive drugs. They are called 'opportunistic' because the things which cause them (eg. organisms such as viruses, bacteria, or fungi) are often commonly present in the body and in the environment.
If you have an intact immune system, these agents will not cause serious infection or illness: the immune system will 'deal with' them. But when the immune system is significantly damaged, for example, by HIV, these common agents may escape the usual immune system controls and use this "opportunity" to cause disease. Opportunistic infections can cause death and debilitating illness.

Generally, the risk of developing an OI increases as a person's CD4 (T-cell) count decreases. Smoking and excessive alcohol use may lead to increased susceptibility to some opportunistic infections, and when they do occur, may result in those infections being more severe and more difficult to treat. The use of combination antiviral therapy to drive down the amount of virus replicating in the blood has meant that many people with HIV, over the last two to three years, have not sustained the serious immune damage responsible for AIDS. So the numbers of people reporting the OIs described below have in most cases dramatically decreased. However, the risk of developing OIs is closely tied to CD4 counts. If you have a low CD4 count, despite your viral load, you could be at risk of developing any of the conditions described below. In particular, if your CD4 count is less than 250, you should consider where appropriate taking drugs for prophylaxis (prevention) against some of the more common and dangerous OIs, like *pneumocystis carinii pneumonia* (PCP). You can talk to your GP or specialist about this. Some research suggests that it may be safe to stop prophylaxis if you have a reasonable and stable CD4 count. However, stopping prophylaxis should only be considered in consultation with your doctor.

Immune restoration disease

Sometimes, people may experience a symptomatic flare-up of an opportunistic infection shortly after starting anti-HIV treatment. This is thought to be part of a phenomenon called immune restoration illness. Sometimes, if a person's immune system has been very damaged, he or she will not get the usual symptomatic and inflammatory reactions to infections. This is because symptoms of illness such as swollen glands, sweats, and so on are a sign that the immune system is in fact doing its job to fight off infection. When people start taking HIV antivirals, they often get a sudden drop in viral load and a slower improvement in CD4 counts. As this happens, they may also experience symptomatic, localised "flare-ups" of underlying conditions and infections such as cytomegalovirus (CMV), bacterial infections or hepatitis, because the immune system is recovering and now able to respond to infection. These "flare-ups" are often treatable, and the symptoms may dissipate over time, as HIV antiviral treatment begins to 'kick in', and improve viral load and CD4 counts.

Role of antiviral therapy

The single most significant factor in changing the epidemiology of AIDS-related conditions, and reducing deaths, was combination antiviral therapy. Talk to your doctor about the role of HIV antiviral treatments if you have questions about this. For many of the conditions you'll find in this booklet, the single most powerful agent to treat or prevent them is effective treatment with HIV antiviral drugs, which control the replication of the virus. HIV antivirals can improve and even alleviate some conditions, as they improve the strength of your immune system.

Part A... HIV and the immune system

What is the immune system?

The immune system is a complicated network of cells and organs which have the primary function of protecting the human body from attacks by "foreign" agents. These can include viruses, infection-causing bacteria, parasites and fungi, or other material introduced into the body - for example, chemicals.
The immune system also acts against the body's own cells where they are already infected by a "foreign" agent, or in the process of transforming from a normal to an abnormal state.
When this system of cells and organs malfunctions, or is impaired, the result can be severe infections, allergy, cancer, or conditions such as AIDS.

What CD4 T-cells do

T-cells are a group of immune system cells responsible for "orchestrating" the way other immune cells respond to infections and other foreign material. Some of these, including the subgroup of T-cells known as T4 (CD4) cells, are responsible for orchestrating the immune response of other cells. Another commonly used name for CD4 cells is "T-helper cells". They are often described as the "generals of the immune army", because they effectively give orders to other parts of the immune system, which actively fight infections.
CD4 cells have their name because they have a specific 'marker', known as a CD4 receptor, on the surface of the cell. They are critical in the body's immune system response.

Immune response and viruses

Typically, if a virus gets into the body of a person with an intact immune system, the following immunologic response follows.
➔The virus is **detected** by macrophages and other immune system cells.
These send out chemical messages activating the immune system, and present the antigen (part of the virus) to a group of immune system cells known as lymphocytes.
➔**The T-lymphocytes (T-cells)** are activated to respond.
➔**The T-cells activate the B-lymphocytes (B-cells)** to produce antibodies, which bind to the virus. Other immune system cells then recognise and destroy the antibody-virus combination.
The antibodies attach to 'free' virus in the blood and other body fluids.
➔**A subset of the T-cells** (some of the CD8 cells) are primed to recognise and destroy cells infected with the virus.
These cells multiply and locate virus-infected cells, and kill them.
➔In many infections, the virus is completely removed from the body through this process, and the immune system **keeps a 'memory'** of the virus.
This means that the body is protected (sometimes only partially, other times completely) against further infection with that virus. This is known as immunity.

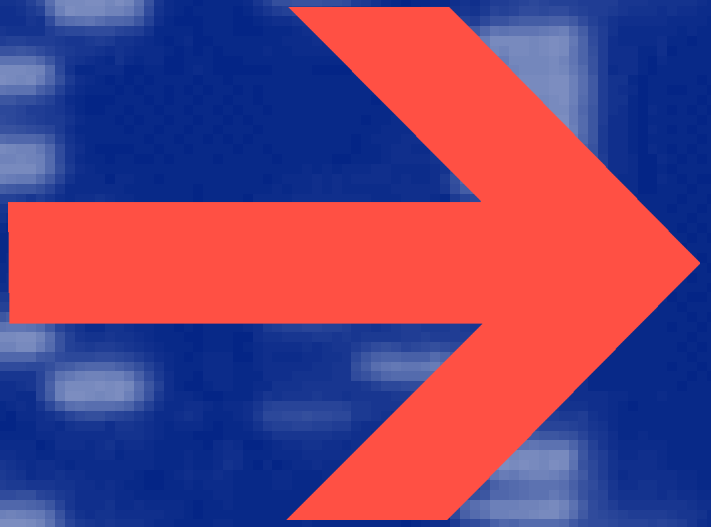
How the body responds differently to HIV

In some viral infections, the immune system cannot completely remove the virus and a chronic infection may occur. This occurs in HIV disease.
What happens is this:
➔HIV **infects cells of the immune system**, replicates **inside these cells** and ultimately destroys them. The immune response to HIV is similar to other viral infections. However, the immune system response is altered because it is the cells of the **immune system itself which are 'infected'.**
➔HIV gets into the body and attaches itself to **CD4 cells**.
➔It **reproduces inside these cells**, ultimately destroying them.
➔The immune system **produces antibodies against HIV** and primes another kind of T-cell, known as a CD8-cell, to recognise cells infected with HIV.
➔These **primed CD8 cells locate CD4 cells infected with HIV** and destroy them.

Why does the immune system get weaker with HIV?

CD4 cells play a crucial role in directing the body's immune response. But if they are infected and subsequently destroyed by virus, the immune response will be generally impaired, and HIV will be free to replicate. This increased production of HIV means increased numbers of CD4 cells are infected and destroyed.
If the rate of CD4 cell infection and subsequent destruction exceeds the body's ability to replace the CD4 cells, then the total number of CD4 cells will decrease, and so too, the ability of the immune system to fight not only HIV itself, but any other unwanted pathogens and foreign material. This weakening of the immune system is what can put a person at risk of opportunistic infection.

Part B... Opportunistic infections and conditions



Viral infections

Cytomegalovirus (CMV)

What is it?

Cytomegalovirus (CMV) is a herpesvirus. Many people, both HIV positive and HIV negative, are likely to have been exposed to CMV during their life. After initial infection with CMV, the virus remains in the body in a latent form, becoming active if and when the immune system is damaged. It is even more common among gay men and injecting drug users. In people with intact immune systems, CMV causes no problems. But if your immune system is not functioning properly, a virus like CMV can cause serious illness.

CMV in people with AIDS can cause a serious eye condition known as retinitis, which can lead to blindness. CMV can also get into the intestine (called *CMV colitis*), the mouth and throat (*CMV oesophagitis*) or the spine (*CMV myelitis*). It can also get into the brain, causing an inflammation known as CMV *encephalopathy*. CMV can also get into the adrenal system (*CMV adrenalitis*) causing a drop in blood pressure and a lowering of adrenal function.

Am I at risk?

If you're positive to CMV and HIV has caused damage to your immune system, you could be at risk of CMV disease.

The risk of CMV causing disease increases with immune damage. People with CD4 (T-cell) counts of less than 100 are at greatest risk. In general, combination antiviral treatment has lead to dramatically reduced instances of this opportunistic infection.

What are the symptoms?

a. *CMV retinitis*

See your doctor, or an eye specialist (opthalmologist) if you have a low CD4 count, and vision problems, in particular, 'flashing' lights, blurred vision, or moving "black spots" on your field of vision. These are known as blind spots (or floaters), and indicate that the retina of your eye is inflamed or damaged. On the other hand, it is possible to have CMV retinitis but no symptoms at all. This is why it is very important to have regular eye checkups if you are in the group of people at risk of CMV.

b. *Colitis, oesophagitis, myelitis*

CMV colitis may be indicated by diarrhoea. Since diarrhoea in people with HIV may be caused by a number of things, CMV mightn't be an obvious suspect. It can be diagnosed in a biopsy, where a small sample of tissue is taken from the intestine, and tested. If you experience difficulty and pain when swallowing, this could be a sign of CMV oesophagitis (the infection is affecting your oesophagus).

If CMV spreads to your spine, you could develop myelitis. The symptoms of this could include weakness, numbness in the spine, tingling in the spine or legs, or pain when walking.

c. *Encephalitis*

Encephalitis refers to the inflammation of the brain. This could be caused by a number of different things, an accurate diagnosis is important. Symptoms such as poor concentration, headaches, inexplicable personality or behaviour changes could suggest CMV encephalitis. CMV encephalitis can be confidently diagnosed by a combination of high clinical suspicion and PCR analysis of spinal fluid obtained by lumbar puncture.

How is it treated?

CMV can't actually be 'cured', even when treated with drugs. But it can be suppressed. There are three drugs used to treat CMV: ganciclovir, foscarnet and cidofovir.

Ganciclovir (Cymevene) is administered as an infusion (directly into the blood) or taken orally in capsules. The capsules are generally used once the initial illness is stabilised by the infusions. Initial treatment can be difficult, because you need to be hooked to a drip. Sometimes this is done in a hospital treatment room or outpatient unit: initially, it will be done every twelve hours for a period of three weeks.

Foscarnet (Foscavir) and cidofovir (Vistide) similarly require infusions.

Despite the above drugs, CMV can and often does recur.

Can I prevent it?

CMV can be transmitted through kissing, or other sexual contact, and is found in breast milk, faeces and urine. All of this explains its relatively high prevalence in the community.

It's impractical and dishonest to make prevention recommend-ations in terms of exposure to the virus. A blood test can determine whether you're CMV positive, but won't tell you whether any current symptoms or problems are caused by the CMV—you'll still need biopsies or other tests for this. Two blood tests determine distinctively if you carry CMV and if the infection is active, these are CMV serology and CMV PCR respectively.

The most useful recommendation is to be aware of its possible symptoms, and to talk to your doctor if you think you are at risk. The earlier you can treat CMV disease, the greater chance you'll have of containing it. Regular eye checkups are one of the most important ways you may prevent CMV— an opthalmologist may detect retinitis before symptoms even occur.

CMV and immune restoration

The risk of symptomatic CMV disease (eg. retinitis) may in fact be greater, in people with severe immune damage, during the first three to six months of treatment with potent combination HIV antiviral therapy.

It is thought that this could be due to immune restoration illness (discussed previously). Continuing treatment with antiviral therapy during this period could be very important.

Progressive Multifocal Leukoencephalopathy (PML)

What is it?

PML, a central nervous system disease, is not a virus itself, but its cause is thought to be viral: the JC virus, a papovirus.
(Papoviruses include the a group of viruses called papillomaviruses, which can cause genital and other warts). It is thought PML occurs because the JC virus is 'reactivated' in a person with a poor immune system.

Am I at risk?

Most people will have been exposed to the JC virus. Despite this, PML is fairly uncommon. However, the risk of developing PML increases with immune system damage.

What are the symptoms?

PML affects the central nervous system, which includes the brain and spine. Its symptoms may overlap with those of other neurological or psychological conditions. PML can cause confusion, disorientation, feeling 'washed out', loss of balance, and speech difficulties (eg. slurring words). Weakness in the limbs of one side of the body may also be a sign, or loss of vision in one eye. PML can quickly become serious and life-threatening.

How is it diagnosed?

Because it shares symptoms in common with other opportunistic illnesses, getting a definite diagnosis is important. Brain scans can assist the diagnosis. The only way to diagnose PML for certain is with a brain biopsy, in which a small sample of brain tissue is removed and tested.
A PML diagnosis might be assisted by testing for the JC virus in the clear fluid which surrounds and circulates through the brain, spine and central nervous system. This is done by a lumbar puncture (spinal tap), in which a needle is inserted into the spine to take a sample.

How is it treated?

PML is pretty hard to treat.
A number of drugs have been considered, or used, including high doses of the HIV antiviral AZT, and anti-herpes drugs such as acyclovir, and anti-CMV drugs.
Treatment with combination antiretroviral therapy, which may prevent severe immune damage, and suppress HIV, is likely to have a long-term role in preventing conditions like PML. In fact, it is the most effective treatment for PML at this point.
HIV antivirals, because they can improve the immune system, may also prolong survival in people with PML. PML may resolve when combination therapy is introduced.
A small percentage of people appear to spontaneously recover from this condition. This is more likely in people with CD4 counts of more than 200.

Cancers and lymphomas

Cervical cancer

What is it?

Cervical cancer is a preventable condition, and if diagnosed at an early stage, can be cured.
Cervical cancer and cervical cell abnormalities affect many women regardless of their HIV status. But evidence suggests that the kinds of cervical cell abnormalities that can lead to cancer are more common in HIV positive women.

Am I at risk?

Not all cervical cell abnormalities (a condition called cervical dysplasia) mean you have cancer or are likely to get it. However, more severe kinds of dysplasia are associated with the development of cancer.
These possibly pre-cancerous changes are graded into three tiers according to their severity: CIN 1, CIN 2, and CIN 3.
(CIN stands for *cervical intraepithelial neoplasia*). Once established, CIN is more difficult to treat in HIV positive women than HIV negative women. This makes early detection for HIV positive women more important.
➔ CIN 1 means there are some mild changes, with a small risk of developing cancer (about 7 percent);
➔CIN 2 changes have about a 50 percent chance of becoming cancerous;
➔CIN 3 changes are severe, and may mean cancer is already present and active.
If you have a pap smear which shows such high-level dysplasia, your doctor should immediately refer you for further tests.
An examination of the cervix called a colposcopy may be recommended.
The cervix is closely examined under a microscope, and cells may be taken for testing. There have been some arguments that this test should be routine in all HIV positive women, but others disagree, saying it is unnecessary unless pap smear results are abnormal. Colposcopy is invasive and may be painful. Some researchers have suggested that progression to cervical cancer may be faster in HIV positive women. Invasive cervical cancer is an AIDS-defining illness.

Other risk factors

➔Some kinds of the human papillomavirus, a sexually transmissible infection which causes genital warts, are strongly linked with cervical cancer. Although the viral subtypes associated with genital warts are different to those associated with cervical dysplasia they can be an indication of risk exposure.
➔Smoking appears to be a risk factor.
➔The risk of developing cervical cancer also increases with age: women may be at increasing risk from their mid-30s.

How is it treated?

Cervical cancer is usually treated by surgery or radiotherapy. The main reason why it is important to detect cervical cancer or pre-cancer early is that it appears current treatments may have a higher likelihood of failure in HIV positive women, especially women who have a low CD4 count.
In addition, abnormal cells which have been treated (eg. through laser surgery) may be more likely to recur.

Can it be prevented?

The main message for HIV positive women in terms of cervical cancer is that early detection is critical. This should include:
➔regular six-monthly pap smears (some people disagree and say only annual smears are necessary);
➔further referral if your pap smear shows abnormal cells;
➔aggressive treatment in the case of severe dysplasia.
Whether or not you've been exposed to genital warts (but especially if you have), you should consider a regular pap smear as essential.
The danger of cancer can be reduced if problems are picked up early. But if there are any problems with your results, or you've had a history of HPV or warts, pap tests every six months are suggested. Talk to your doctor about the options.
HPV occurs through skin contact with infected areas. If you know you've never been exposed to the virus, you can reduce the likelihood of contracting HPV by using condoms and other protection, like dams, during sex.

Kaposi's Sarcoma

What is it?

Kaposi's Sarcoma (KS) consists of individual cancerous lesions, caused by an overgrowth of blood vessels.
KS may appear as pink or purple lesions on the skin, but can also develop in body cavities such as the throat, intestines and lungs.

Am I at risk?

KS is caused by a herpesevirus, called human herpesvirus 8.
Many people suggested that Kaposi's Sarcoma was caused by a sexually transmitted agent because:
➔Gay men have a higher incidence of HHV8 positivity, suggesting that it could be linked to certain sexual practices. This remains unconfirmed.
➔Gay men with HIV were far more likely to develop KS than other positive people.
➔Only low rates of KS are found among injecting drug users and people with haemophilia, suggesting that blood-to-blood contact may be a poor route of transmission.
➔Cases of benign KS have been observed in HIV negative gay men who have no immune dysfunction.
➔The risk of developing KS for a woman with HIV is closely related to her partner's. Female partners of gay or bisexual men are more likely to develop KS than other positive women. There has been a significant decline in the number of gay men developing KS, most likely due to the long-term practice of safe sex, and to antiviral treatment improvements.

What are the symptoms?

KS may present as an incidental condition (eg. the appearance of lesions on the face, genitals or legs) through to rapidly aggressive tumour growth causing death in some cases.

How is it diagnosed?

KS is diagnosed by biopsy of a skin lesion, or a presumptive diagnosis is made on the basis of its appearance. Today, most doctors recommend a biopsy to be sure.

How is it treated?

Some of the treatments used specifically for KS are:
➔freezing the lesions (cryotherapy);
➔injections directly into the lesion;
➔radiation therapy;
➔daunorubicin hydrochloride (a kind of injectable chemotherapy);
➔doxorubicin hydrochloride (a kind of injectable chemotherapy).
The most effective treatment for KS, however, is successful anti-HIV treatment, which will improve your CD4 count and immune system.

Non-Hodgkin's Lymphoma

What is it?

Non-Hodgkin's Lymphoma (NHL) is a cancer where immune system cells known as B-lymphocytes multiply out of control. NHL is classified in two ways; systemic and primary CNS lymphoma. Systemic lymphoma occurs in the lymph node system, while primary CNS lymphoma occurs in the spinal cord and brain.

Am I at risk?

It's not clear what causes NHL. It is associated with overactive B-lymphocytes. It has been speculated that B-cells might become overactive if they are being stimulated by the consistent presence of viruses or other organisms. Viruses such as Epstein-Barr and HHV8 have been commonly found in people with NHL.
While the rates of many opportunistic infections have declined dramatically since widespread use of antiviral drugs, it is not clear that there has been such a similarly significant decline in systemic NHL.

What are the symptoms?

The symptoms of NHL may actually be similar to the symptoms of a number of other neurological conditions, some related to HIV.
But NHL can be diagnosed through testing of bone marrow samples, the cerebrospinal fluid (CSF: a fluid which protects the

brain and spine), or other tissues where the condition is suspected.
Common symptoms of NHL include:
➔weight loss;
➔fever;
➔enlarged lymph nodes;
➔severe nightsweats;
➔neurological disturbances including headaches, confusion, memory loss, paralysis down one side of the body, speech and comprehension problems.
Since many of these symptoms are non-specific, other causes need to be ruled out.
With respect to differential diagnosis, systemic lymphoma can mimic the symptoms of CMV or MAC, whilst CNS lymphoma can mimic CNS toxoplasmosis.

How is it treated?

NHL is notoriously difficult to treat. When lymphoma is concentrated in the brain, it is often treated with radiotherapy. Chemotherapy drugs may also be used.
Treatment of non-nervous system lymphoma involves cycles of chemotherapy with a combination of agents.

Fungal, bacterial & protozoal infections

Candidiasis

What is it?

Candida albicans is a naturally occurring yeast which usually lives in harmony with its human host in the gut, the folds of the skin, the anus, the mouth and the vagina. Candidiasis occurs when the balance of this yeast is disturbed.

Am I at risk?

There is always some *candida albicans* living in the body, but it can 'multiply' to above normal levels when there is a change in the vaginal environment (for example, in sugar or pH levels). Generally, the yeast is controlled by its host. But if the immune system is compromised, the host can lose control of the organism, and it starts to behave like a disease.
Vaginal candidiasis is an exceptionally common infection in all women, regardless of HIV status. Chronic, or very frequently recurring, vaginal candidal infection is the most common gynaecological disorder in women with HIV.
Candidiasis can also occur in other parts of the body (the mouth and the oesophagus). This is more common as immunosuppression increases.

What are the symptoms?

Oral candidiasis may appear as white patches on the tongue and mouth membranes (eg. the inner cheeks).
Vaginal thrush occurs far more frequently, and with greater severity, among HIV positive women. Symptoms include crotch-itch, tiredness, and a furry, white, usually odourless vaginal discharge.
Men may experience thrush *under the foreskin.*
Oesophageal candidiasis is caused by the overgrowth of candida in the oesophagus (the passage leading from the back of the throat to the stomach).
It can be painful and debilitating, causing difficulty in swallowing and chest pain. In severe late-stage disease, candida growth can also affect the *brain or lungs*, though this is relatively rare. If candidiasis is very severe, it can cause fevers, sweats and weight loss.

How is it diagnosed?

Candida in the mouth can be diagnosed by the simple examination of the mouth. Suspected candida growth in areas such as the oesophagus or brain may be confirmed by biopsy or culture.

Can I prevent it?

Women being treated for candidiasis may be re-infected by male partners during unprotected sex. The amount of candida in the vagina will be far greater than the number of spores likely to be found under the foreskin.

How is it treated?

a. *Topical antifungal agents*
There are a range of topical anti-fungal agents, some of them natural therapies, which may assist in treating vaginal thrush, thrush under the foreskin, or under the fingernails.
These include:
➔live yoghurt which contains the bacteria *lactobacillus acidophilus* — some practitioners maintain that the bacteria in commercial *acidophilus* yoghurt is ineffective;
➔broad-spectrum anti-fungal creams or powders such as Canesten. These are available from your chemist.
You won't need a prescription, but you will have to pay for these products: topical antifungals have been removed from the Schedule of Pharmaceutical Benefits.
➔Amphotericin lozenges
b. *Systemic treatment*
For more serious candidiasis, oral antifungal drugs may be used.
These include:
➔fluconazole;
➔ketaconazole;
➔itraconazole.
Severe candidiasis is treated with intravenous amphotericin.
Sometimes, this is given as a drug called liposomal amphotericin B, where the potent anti-fungal amphotericin B is presented in a solution of liposomes (a kind of fat), in order to reduce the strain on the kidneys.
c. *Anti-candida diets: do they have a role?*
You may have heard that candida can be managed by special diets,

which eliminate foods supposed to cause candida.
However, many doctors believe there is no evidence that these diets have any impact on candidiasis, and warn they can be dangerous in positive people because of the potential for weight loss. It does make sense in general to eat well, and eat regularly. Variety in your foods is really important for a healthy diet. One of the problems with many anti-candida diets is that they often restrict a number of foods (like bread), which help maintain weight and energy. These are restricted because they contain yeast. However, it's not clear that there is a link between eating foods with yeast, and the development of candidiasis. If you are going to embark on an anti-candida diet, it would be worth making sure you are still eating a wide enough variety of fresh, energy-dense foods, such as grains.

Crytosporidiosis

What is it?
Cryptosporidia are small parasites, which occur commonly in the environment.
The condition caused by this organism is known as *cryptosporidiosis*, often identified by a watery, persistent diarrhoea. The organism exists in animals, food and water, and can rarely be transmitted between people.

Am I at risk?
Cryptosporidia occur commonly in water and throughout the environment. Contact with faeces is one way in which crypto-sporidial infection is thought to be spread. Avoiding activities such as unprotected rimming may be a practical preventative measure.
It is important for people with HIV, particularly if you have a low CD4 count, to consider boiling drinking water, or using sealed bottled water, since cryptosporidiosis is notoriously difficult to treat.

What are the symptoms?
Cryptosporidiosis can also affect immune competent people on an acute basis, causing an acute watery diarrhoea. However, these symptoms resolve without treatment.
Positive people who have low CD4 counts usually have chronic (ongoing) illness, which cause:
- watery diarrhoea (generally non-bloody);
- abdominal pain and cramping;
- nausea;
- weight loss.

How is it diagnosed?
Cryptosporidia are usually detected by taking a sample of faeces for testing.
They can also be detected through a rectal biopsy or, less usually, an intestinal biopsy.

How is it treated?
Acute cryptosporidiosis generally doesn't require specific treatment, and will clear up of its own accord. But treating chronic cryptospor-idiosis is difficult. The most effective treatment is to improve CD4 counts using antiviral treatment. Unlike many HIV related opportun-istic illnesses, there is no standard of treatment. Many drugs have been tried, including common antibiotics used for other fungal and parasitic infections.
In Australia, the most common and reasonably effective treatment is an antibiotic called paromomycin.
In the absence of effective drugs, treating symptoms becomes important. Anti-diarrhoaea drugs such as Imodium and codeine can be used, and pain relieving and anti-spasmodics may relieve symptoms.

Travel
Cryptosporidia occur commonly in water supplies. If you are travelling overseas, particularly in countries where you are not sure about the quality of the local water supply, it is extremely important to ensure that all drinking and cooking water is boiled or consumed from sealed bottles.

Microsporidiosis

What is it?
Microsporidia are small parasites, which occur commonly in the environment. The organism exists in animals, food and water, and can be transmitted between people. Rimming may be a risk factor for transmission of microsporidia. The disease caused by this organism when it multiplies out of control is known as microsporidiosis, often identified by a watery, persistent diarrhoea.

Am I at risk?
There is some debate about the ways in which people become infected by these protozoa, but rimming and other sexual activities involving faecal contact may play a part. Avoiding activities such as rimming without a dam or other protection may be a practical preventative measure.

What are the symptoms?
- watery diarrhoea;
- abdominal pain and cramping;
- weight loss.

How is it diagnosed?
Microsporidia can be difficult to detect, because of their small size.
A diagnosis often requires a small bowel biopsy, which is invasive and can be unpleasant. There are new techniques which make diagnosis simpler, through, for example, examining faecal matter under a special microscope or using a special stain.

How is it treated?
The most effective treatment is to improve CD4 counts using antiviral treatment.
Microsporidiosis is hard to treat, and there is no approved standard of care. A number of broad spectrum antibiotics and anti-parastics which have been used with varying degrees of success including metronidazole (Flagyl). Combination antiviral therapy can improve symptomatic chronic microsporidiosis, because of associated improvements in the immune system.

Mycobacterium Avium Complex (MAC)

What is it?

MAC is caused by two similar mycobacteria. Both occur commonly in the environment, for example, in water, soil, dust and some animals. The bacteria are known as *Mycobacterium avium* and *Mycobacterium intercellulare*.

In a person with HIV and very low CD4 counts, these organisms can multiply unchecked in the body, and infect key organs, including the spleen, the lymph nodes, bone marrow, lungs and intestinal tract.

Am I at risk?

MAC is a definite risk for people with very low CD4 counts (usually below about 75 CD4 cells). It is difficult to avoid exposure to the bacteria which causes MAC.

People with a poor immune system may continue to be at risk of symptomatic MAC infection for up to six months after starting to take HIV antivirals. It is thought that this is because the mycobacteria which cause the condition often sit undetected in body tissue, such as the gut wall or lymph nodes.

If HIV antivirals cause improvements in immune response, the immune system may mount an attack on the MAC organisms, and so cause symptoms of an inflammatory immune response against these local outbreaks.

But if a person is severely immunodeficient, the organisms may multiply out of control, unchecked by an immune response, and may spread into the blood and other tissues and organs: this is known as *disseminated* MAC.

Symptoms

Symptoms of MAC are generally non-specific. They may include: anaemia; lymph node swelling; fever; nightsweats; fatigue; loss of appetite; weight loss; abdominal pain and diarrhoea.

How is it diagnosed?

MAC is diagnosed through a blood or tissue culture.

Can I prevent it?

If you have a low CD4 count, especially one of less than 100, you should take the risk of MAC seriously. Talk with your doctor.

Two drugs, clarithromycin and azithromycin are approved as propyhlaxis against MAC, for people whose CD4 counts are 50 or less.

How is it treated?

If disseminated MAC infection is definitely diagnosed, it is usually treated with a combination of drugs. The drugs used include clarithromycin (sold as Klacid), plus a drug called ethambutol, plus rifabutin. Once commenced MAC treatment should continue indefinitely.

Pneumocystis carinii pneumonia (PCP)

What is it?

This infection of the lungs is caused by an organism called *Pneumocystis carinii*. In the early years of the HIV epidemic, PCP was one of the most commonly fatal opportunistic illnesses. Improved treatment and prophylaxis have dramatically reduced PCP mortality rates.

Am I at risk?

People with CD4 cell counts of less than 200 are at greatest risk for developing PCP. People who have already had PCP are at risk of the infection recurring, especially if they have a low CD4 count. The US Centers for Disease Control recommends all people with HIV should receive prophylaxis against PCP if you have less than 200 CD4 cells, unexplained fever, or a history of candidiasis in the mouth or throat.

The risk of developing PCP is greater when HIV remains untreated or undiagnosed.

The overall numbers of people with PCP in Australia have declined.

But PCP is often the first sign of HIV infection, in people who do not know their HIV status, because it occurs at a relatively higher CD4 count than some other infections. HIV testing and treatment where appropriate remain important in preventing PCP.

What are the symptoms?

Symptoms of possible PCP should be checked out straight away.

They include:

- high fever;
- shortness of breath;
- tightness or pain in the chest and lungs;
- cough; (onset gradually and persistent)
- weight loss.

How is it diagnosed?

Often, a diagnosis of presumed PCP can be made on the basis of the symptoms, taking into account a person's CD4 count, or using chest x-rays.

Detection of the organism through a bronchoscopy or special sputum test will confirm a diagnosis.

Can I prevent it?

Yes, PCP can be prevented.

The preferred drug is trimpethoprim-sulfamethoxazole (a type of antibiotic which includes Bactrim and Septrin).

About 50 percent of people have adverse reactions to the sulphur in these drugs, sometimes severe. You can be 'desensitised' if your reaction is not a serious one.

Alternative prevention measures may include a drug called aerosolised pentamadine (which you have to breathe as a 'mist' through a special mask).

This can only be done in a hospital or outpatients treatment unit.

It should be done about once every four weeks, and takes about 45 minutes.
It seems that pentamadine is less effective at preventing PCP than Bactrim or Septrin. But even if these drugs are used, PCP can sometimes develop.
Some recent research has associated the development of PCP with not taking prophylaxis, but also with poor adherence to antiviral drug regimes.

How is it treated?
PCP can be treated with: the antibiotics Bactrim and Septrin. Treatment is for three weeks at least. Treatment for PCP is often commenced in hospital, but can be continued as an out-patient if the doctor determines that there has been adequate improvement.

Pneumococcal pneumonia

What is it?
Pneumococcal pneumonia is actually the lung inflammation most people know as common old "pneumonia". This most common type of pneumonia is caused by infection with a kind of bacteria, called *Streptococcus pneumoniae*, which infects the lungs: it is also called *pneumococcus*. Pneumococcal pneumonia is not usually thought of as an HIV-related condition, since it is a bacterial infection not uncommon among many groups of people, including the elderly, or people with poor health or lowered immunity. However, people with HIV are a group of people likely to be particularly at risk of developing this kind of pneumonia, and are more likely to have recurrent pneumonia.

Am I at risk?
Many people without HIV also get pneumonia from pneumococcal infections.
There are a number of additional factors which may increase a person's risk of developing pneumococcal pneumonia, including:
- smoking;
- breathing in chemical irritants;
- flu.

What are the symptoms?
This kind of pneumonia may share some of the same symptoms as PCP, including:
- fever;
- sweats;
- a cough which may be initially dry and not produce much sputum, but which may later be green or dark yellow.

How is it diagnosed?
Pneumococcal pneumonia is often diagnosed with a chest x-ray, but this will not necessarily tell you what the organism causing the pneumonia is. The symptoms often overlap with other chest infections, including not only PCP, but other lung problems and conditions. Sometimes, cultures can be used to test for and identify the pneumonia-causing organism.
In some circumstances, for example, where there is a clear epidemic or outbreak of pneumonia in a particular environment or setting, a presumptive diagnosis might be made.

Can I prevent it?
A vaccine against pneumococcal infection is available, which is administered by a single injection into the muscle (like a tetanus shot). It is usually not used for HIV, however, because many people feel it is not only less effective, but could be dangerous. You could talk to your doctor about whether this vaccination would be appropriate.
Bactrim, used for the prophylaxis of PCP, offers significant prophylaxis against bacterial pneumonia.

How is it treated?
Bacterial pneumonia is treated using antibiotics (like penicillin or erythromycin), which can be taken orally, by infusion in hospital, or a combination of the two.
For more severe cases, newer classes of very broad spectrum antibiotics, which are stronger and effective against a wider range of organisms, may be used.

Toxoplasmosis

What is it?
This condition, which can manifest itself as toxoplasmic encephalitis (inflammation in the brain) is caused by a parasite called *toxoplasma gondii.* The organism may also affect other organs, including the lung, eye, skin, heart and gastrointestinal tract.

Am I at risk?
The *toxoplasma gondii* organism can be found in raw and undercooked meats, some other food products (such as eggs), and some animals. Cat excrement, particularly kitten excrement, has been implicated as an environmental source of the infection, which will not generally present any symptoms in people with intact immune systems. People with CD4 counts of less than 100 are at greatest risk.

What are the symptoms?
Common symptoms of toxoplasmosis include:
- seizures;
- fever;
- dull and persistent headache;
- confusion;
- lethargy;
- other possible neurological symptoms, including weakness, paralysis of one side of the body, speech disorders and problems with walking and balance.

How is it diagnosed?
Toxoplasmosis can be difficult to diagnose. This is because its symptoms may be similar to other

neurological disorders. Blood tests and CT brain scans can be used.
A brain biopsy will give the most rapid and unambiguous diagnosis, but this procedure is invasive, and is usually only done when someone with suspected toxoplasmosis is not responding to treatment.

Can I prevent it?

With the exception of pentamadine, the agents likely to offer effective prophylaxis against toxoplasmosis include those also used to prevent PCP (eg. Bactrim, Septrin).
There are some practical measures advised for minimising your risk of being exposed to the organism which causes toxoplasmosis. If you're cooking meat, make sure it's thoroughly cooked through at a high temperature. Raw or undercooked meat should be avoided.
If you have a cat, avoid contact with cat excrement or litter. Always use gloves if you are changing the litter tray: preferably, get someone else to do it. Feed your cat commercially prepared dry or tinned food, and avoid handling undercooked meat. Wash any raw vegetables well. Avoid contact with garden soil: wash your hands if you've been in the garden.

How is it treated?

Drugs used to treat toxoplasmosis may include: pyrimethamine in combination with a sulphadiazine. The antibiotic clindamycin plus pyrimethamine may be used by people who are intolerant to the sulphur-based drugs like Bactrim and Septrin.
It is necessary to take daily treatment to control and suppress the parasite to prevent recurrence. This will usually consist of lower doses of some of the drugs discussed above. Once commenced, treatment for toxoplasmosis continues indefinitley.

Travel

Toxoplasmosis is often present in the environment. If you are travelling overseas, or anywhere where you don't have much control over the environment in which your food is being cooked and handled, try and make sure that any meat you eat is thoroughly cooked.

Tuberculosis (TB)

What is it?

Tuberculosis is an infection which, up until recent times appeared to be generally controlled in the developed world. However in recent years there have been cases of multi-drug resistant TB reported in the United States. Tuberculosis is caused by a bacteria which is carried in the air. The infection commonly occurs in the lungs, though it can affect other parts of the body including the spine.

Am I at risk?

Exposure to TB is fairly rare within Australia, however if you have lived in or have immigrated from South East Asia or have been in contact with people who have TB then you are at risk.

What are the symptoms?

Often there are no symptoms but the active infection can be characterised by fevers, cough and or back pain.

How is it diagnosed?

Infection with TB can be diagnosed from a chest x-ray and or a sputum sample or what is known as a Mantoux test. The Mantoux test involves the injection of a small amount of tubercluin (bacteria) under the skin to see if a reaction occurs within 24 hours.

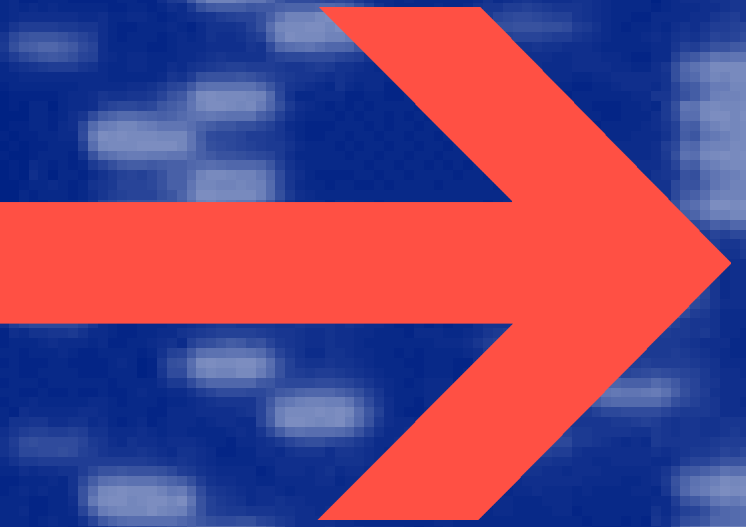
Can I prevent it?

The only way to prevent infection with TB is to avoid situations where you could possibly be exposed to the bacteria. However, people with HIV who have been exposed to TB can prevent later developing symptoms of TB by taking a course of prophylaxis. This is particularly important for positive people as the infection can become active as t-cells decline.

How is it treated?

The infection is treated with a combination of antibiotics. Isoniazid, rifampin and pyrazinamide or rifabutin and pyrazinimide. A decision to use a regimen containing either rifampin or rifabutin should be made after careful consideration with your doctor of potential drug interactions, especially those related to protease inhibitors and non-nucleoside reverse transcriptase inhibitors.

Part C... Prophylaxis



Prophylaxis in the antiviral age

Before combination HIV antiviral drugs were widely used, people with HIV who had low CD4 counts, or who had been diagnosed with AIDS-defining conditions, were often advised to consider prophylaxis against the more common infections, especially PCP and MAC.

Prophylaxis means you take a drug presumptively, without necessarily having had a diagnosis of a particular condition, in the knowledge that you are at high risk of this infection.
The idea is that the drug prevents the infection.

It was the widespread use of antibiotics to prevent people developing PCP which was the first real breakthrough in preventing AIDS deaths in the 1980s.

Improvements to the immune systems of many positive people, through treatment with antivirals, have meant that the visibility of many AIDS-related conditions has decreased. So, too, has the practice of prophylaxis.

There have been some debates about when and if prophylaxis should be considered by people taking HIV antivirals.
The pill burden of many combinations of treatment is already high, and obviously no one – doctor or patient – wants to add to that with more unnecessary pills.
More pills also means a greater risk of unexpected drug interactions.

It's usually the practice now not to automatically introduce prophylaxis at a particular "point", but to take account of a person's overall situation and health, including viral load, CD4 count, the lowest your CD4 count has ever been (called the nadir point), and previous AIDS-defining illnesses you might have had.

If, for example, you have a stable viral load and a reasonable CD4 count (say, above 350), you could reasonably consider stopping prophylaxis, but this decision needs to be considered with your doctor. If, with your doctor you decide to discontinue prophylaxis it is recommended that regular monitoring is maintained.

On the other hand, people who have ever had a really low CD4 count (say, less than 100), might be advised to remain on prophylactic drugs, especially if you have ever had specific infections before.

Prophylaxis and treatment breaks

One time when it might make sense to consider prophylaxis is if you are taking a break from antiviral therapy and have a lower CD4 count.
The risk of developing an OI in the absence of treatment can increase. However, you may need to weigh up this risk against other factors (such as the reason you stopped treatments). Some people stop treatments for a while because they are sick of taking pills: so it may be difficult to suggest that you take a "break", but paradoxically, take pills during this time. Nonetheless, the pill burden of prophylaxis is substantially lower than most combination therapy, so it is something to be seriously considered, given the potential severity of some OIs.
If you are taking a treatment break, one of the best ways to know if you are at risk of developing an OI is to monitor your CD4 count and viral load regularly, keep track of any unexpected or sudden changes, and be aware of any symptoms, particularly extreme tiredness, sweats, diarrhoea or visual problems, which might suggest an OI.

Often, people are worried about discussing treatment breaks with their doctors. But many doctors have experience with people taking breaks, and working with patients through this. Monitoring CD4 count, viral load and possibly other markers at least monthly is important. The risk of developing an OI may be significantly lessened through this.

For further information contact your local AIDS Council or PLWHA group

ACT

PLWHA (ACT)	**(02) 6257 4985**
AIDS Action Council of ACT	**(02) 6257 2855**

NSW

PLWHA(NSW)	**(02) 9361 6011**
AIDS Council of NSW	**(02) 9206 2000**

Northern Territory

PLWHA(NT)	**(08) 8941 1711**
AIDS Council of Central Australia	**(08) 8953 1118**
NT AIDS Council	**(08) 8941 1711**

Queensland

Queenland Positive People (QPP)	**(07) 3846 3939**
Queensland AIDS Council	**(07) 3017 1777**

South Australia

PLWHA(SA)	**(08) 8293 3700**
AIDS Council of SA	**(08) 8362 1611**

Tasmania

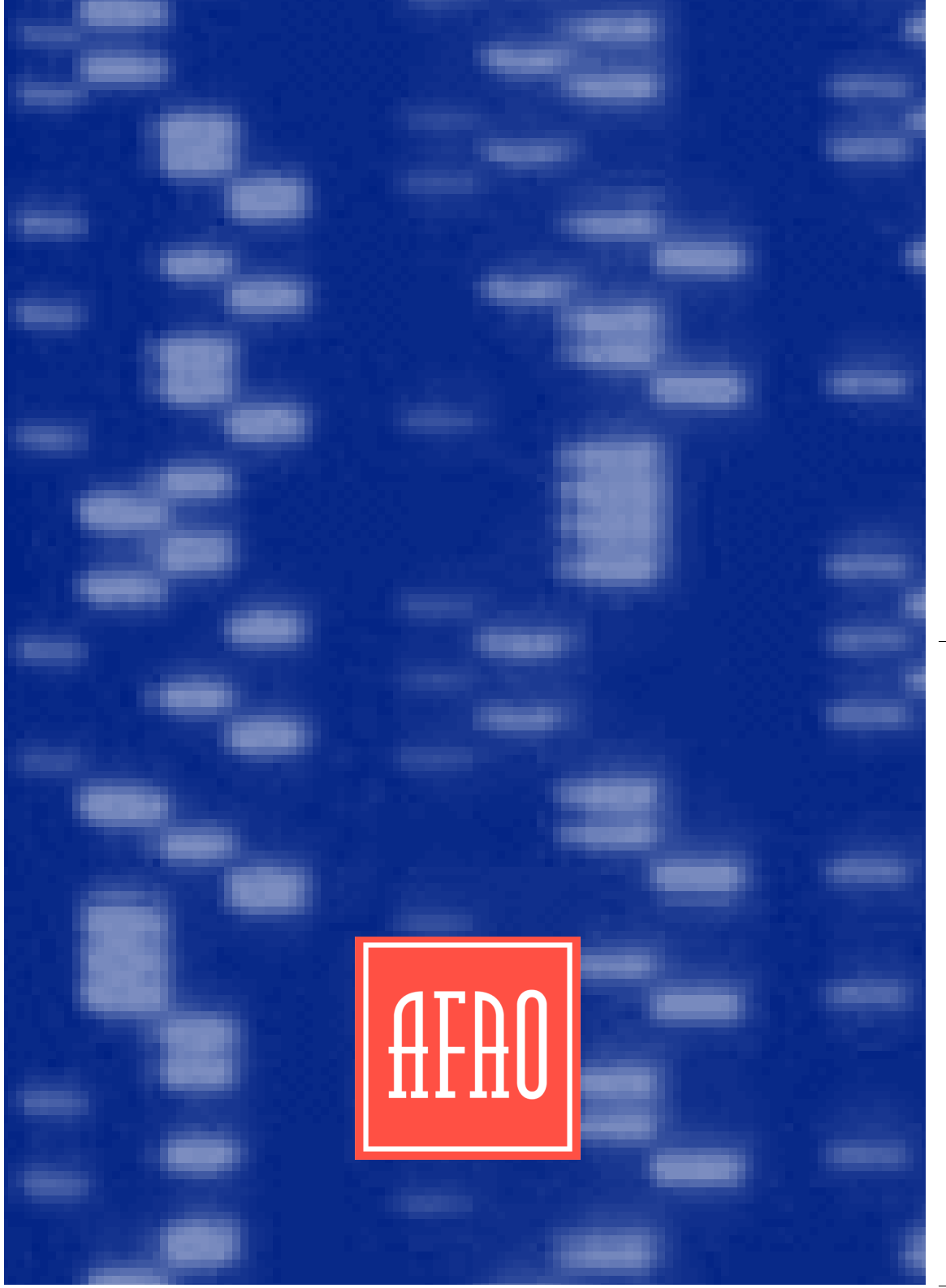
Positive People Tasmania	**(03) 6234 1242**
TasCAHRD	**(03) 6234 1242**

Victoria

PLWHA (Vic)	**(03) 9865 6772**
Victorian AIDS Council	**(03) 9865 6700**

Western Australia

Western Australian AIDS Council	**(08) 9429 9900**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