



# AIDS Dementia Complex

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Dementia is a brain disorder that affects a person's ability to think clearly and can impact his or her daily activities. AIDS dementia complex (ADC)—dementia caused by HIV infection—is a complicated syndrome made up of different nervous system and mental symptoms. These symptoms are somewhat common in people with HIV disease.

The frequency of ADC increases with advancing HIV disease and as CD4+ cell counts decrease. It is fairly uncommon in people with early HIV disease, but it's more common in people with severely weakened immune systems and symptoms of advanced disease. Severe ADC is almost exclusively seen only in people with advanced HIV disease.

ADC consists of many conditions that can be of varying degrees and may progressively worsen. These conditions can easily be mistaken for symptoms of other common HIV-associated problems including depression, drug side effects or opportunistic infections that affect the brain like toxoplasmosis or lymphoma. Symptoms of ADC may include poor concentration, forgetfulness, loss of short- or long-term memory, social withdrawal, slowed thinking, short attention span, irritability, apathy (lack of caring or concern for oneself or others), weakness, poor coordination, impaired judgment, problems with vision and personality change.

Because ADC varies so much from person to person, it is poorly understood and has been reported and described in many conflicting ways. This publication will shed light on some of these issues as well as the available treatments for ADC.

### Possible Symptoms of Early Stage ADC

- Difficulty concentrating
- Difficulty remembering phone numbers or appointments
- Slowed thinking
- Longer time needed to complete complicated tasks
- Reliance on list keeping to help track daily activities
- Mental status tests and other mental capabilities may be normal
- Irritability
- Unsteady gait (walk) or difficulty keeping balance
- Poor hand coordination and change in writing
- Depression

### Possible Symptoms of Middle Stage ADC

- Symptoms of motor dysfunction, like muscle weakness
- Poor performance on regular tasks
- More concentration and attention required
- Slow responses and frequently dropping objects

- General feelings of indifference or apathy
- Slowness in normal activities, like eating and writing
- Walking, balance and coordination requires a great deal of effort

### Possible Symptoms of Late Stage ADC

- Loss of bladder or bowel control
- Spastic gait, making walking more difficult
- Loss of initiative or interest
- Withdrawing from life
- Psychosis or mania
- Confinement to bed

### What Is ADC?

ADC is characterized by severe changes in four areas: a person's ability to understand, process and remember information (*cognition*); behavior; ability to coordinate muscles and movement (*motor coordination*); or emotions (*mood*). These changes are called ADC when they're believed to be related to HIV itself rather than other factors that might cause them, like other brain infections, drug side effects, etc.

In ADC, *cognitive impairment* is often characterized by memory loss, speech problems, inability to concentrate and poor judgment. Cognitive problems are often the first symptoms a person with ADC will notice. These include the need to make lists in order to remember routine tasks or forgetting, in mid-sentence, what one was talking about.

*Behavioral changes* in ADC are the least understood and defined. They can be described as impairments in one's ability to perform common tasks and activities of daily living. These changes are found in 30–40% of people with early ADC.

*Motor impairment* is often characterized by a loss of control of the bladder; loss of feeling in and loss of control of the legs; and stiff, awkward or obviously slowed movements. Motor impairment is not common in early ADC. Early symptoms may include a change in handwriting.

*Mood impairments* are defined as changes in emotional responses. In ADC, this impairment is associated with conditions, such as severe depression, severe personality changes (*psychosis*) and, less commonly, intense excitability (*mania*).





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## The Symptoms of ADC

Properly diagnosing ADC is heavily dependent on the keen judgment of doctors, often together with specialists like psychiatric, brain or neurology experts. It's easy to imagine how difficult it is to determine impairments in mood and behavior since there's no standard or common course of ADC. In one person it may be very mild with periods of varying severity of symptoms. In another it can be abrupt, severe and progressive. Currently, there is no way to tell how a person will progress with ADC.

Sometimes symptoms of ADC are overlooked or dismissed by caregivers, who may believe the symptoms are due to advanced HIV disease. In fact, people with advanced disease generally do not have symptoms of ADC but do have fairly normal mental functioning as long as they also have no other neurological problems. At the other end of the spectrum, ADC should be carefully distinguished from severe depression—common among people with HIV that may result in symptoms similar to ADC.

ADC occurs more commonly in children with HIV than with adults. It presents similarly and is often more severe and progressive.

## How Does HIV Cause ADC?

While it is clear that HIV can cause serious nervous system disease, how it causes ADC is unclear. In general, nervous system and mental disorders are caused by the death of nerve cells. While HIV does not directly infect nerve cells, it's thought that HIV can somehow kill them indirectly.

Macrophages—white cells that are prevalent in the brain and act as large reservoirs for HIV—appear to be HIV's first target in the central nervous system. HIV-infected macrophages can carry HIV into the brain from the bloodstream. Test tube studies offer these hypotheses about how macrophages may help destroy nerve cells:

An infected macrophage in the brain may shed a particle on HIV's outer coat (called gp120), causing damage to nerve cells.

HIV's TAT gene, which helps produce new virus, detaches from HIV and circulates in the blood, causing toxic effects in nerve cells.

The macrophage itself releases a number of substances that, in excess, can be toxic to the brain. Some examples are quinolinic acid and nitric oxide, among an array of other signal molecules. These can bind to nerve cells and cause cell dysfunction or death. Research has found higher levels of quinolinic acid and other markers of cell activation in the CSF of people with ADC.

HIV infection of other brain cells, including astrocytes.

## What if I think I have ADC?

- Don't be afraid to tell your doctor or any other providers that you suspect something is wrong. If you don't have a doctor or need help finding one, contact local AIDS organizations for help in getting one. They can also help you find a doctor for a second opinion if you need one.
- Keep a small notepad with you and write down your symptoms whenever they occur. This information will greatly help your doctor to help you.
- Build as much support as possible, including friends, family and professionals. Although it's possible to treat ADC successfully, it may take awhile for some symptoms to go away.

## Incidence

Anecdotal reports indicate that there are fewer people with ADC since anti-HIV therapy became standard. People who develop ADC today tend to be "sicker" than those who developed it before the use of anti-HIV therapy. One early study from England supports this theory.

The British study found that only 2% of people with AIDS taking AZT developed ADC from 1982–1988, compared to 20% of those not on AZT. The incidence of ADC dropped from 53% in 1987 (before the arrival of AZT) to 3% in 1988 (after the arrival of AZT).

Early in the epidemic, many new AIDS cases were attributed to ADC. These newly-diagnosed people often had ADC but no other AIDS-related condition. Many doctors report that they are no longer seeing people who have just ADC. It has increasingly become a disease of late-stage AIDS when people suffer from multiple infections.

## Diagnosing ADC

Three tests are required to diagnose ADC accurately: a mental status exam, one of the standard scans (CT and/or MRI) and a spinal tap. These may also help tell ADC apart from other brain disorders like toxoplasmosis, PML (*progressive multifocal leukoencephalopathy*) or lymphoma. Care should be taken, however, as ADC may occur along with the symptoms of other brain disorders. Diagnosing both conditions at the same time can be more difficult.

The main way to detect and evaluate ADC is through a mental status exam. The examination is designed to reveal problems like short- or long-term memory loss, problems with orientation, concentration and abstract thinking as well as swings in mood. Imaging of the brain with scans (like an x-ray) is also used. Certain lab tests can also be useful like examining cerebrospinal fluid (CSF), obtained by a spinal tap (also called lumbar puncture).



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CT and MRI scans are routinely used in the detection of ADC. CT scans are x-rays that use special beams to produce detailed images of organs and structures within the body. In people with ADC these scans usually show signs of destroyed brain tissue. MRI, or *Magnetic Resonance Imaging*, is a sensitive brain scan that is used when CT findings are not conclusive. Results from both of these tests are helpful in ruling out other causes for the symptoms.

Tests of CSF may help determine if someone has ADC, but they are not conclusive. Mostly they're used to rule out other causes of the symptoms of ADC, and that's why they're important. Many people with ADC have higher levels of certain proteins or white blood cells in their CSF. However, not everyone with these levels turn out to have ADC. Also, people with advanced ADC are generally more likely to have higher HIV levels in their CSF, although people with no symptoms of brain disorders sometimes have high HIV levels in their CSF.

## Treating ADC

The best therapies to treat ADC appear to be anti-HIV drugs, and high-dose AZT is the most studied drug for it. However, many specialists contend that how well a potent regimen controls HIV reproduction overall is more important than the actual drugs used in the regimen. This may or may not include using standard, or even high-dose, AZT as part of the regimen.

Generally speaking, creating an anti-HIV regimen with the extra goal of treating ADC follows three basic principals:

1. Start a potent regimen (usually 3 drugs) to decrease HIV levels to below the limit of detection of viral load tests;
2. In people who have used anti-HIV therapy before, consider the prior therapy history as well as information from anti-HIV resistance tests;
3. If possible, use anti-HIV drugs that cross the blood-brain barrier as part of a combination therapy regimen.

It's believed—based on findings that high-dose AZT (1,000–1,200mg/daily) can cross the blood-brain-barrier and effectively treat ADC—that an anti-HIV drug that crosses the blood-brain barrier might help prevent or treat ADC. To date, AZT is the best understood treatment available for ADC. Several groups have reported improvements in

## Drug ID Chart

GENERIC NAME	TRADE NAME
<b>Protease Inhibitors</b>	
amprenavir	Agenerase®
indinavir	Crixivan®
lopinavir	Kaletra®
nelfinavir	Viracept®
saquinavir hard gel	Invirase®
saquinavir soft gel	Fortovase®
ritonavir	Norvir®
<b>NNRTIs (Non-Nucleoside Reverse Transcriptase Inhibitors)</b>	
delavirdine	Rescriptor®
efavirenz	Sustiva®
nevirapine	Viramune®
<b>NRTIs (Nucleoside Analog Reverse Transcriptase Inhibitors)</b>	
lamivudine (3TC)	Epivir®
abacavir	Ziagen®
zidovudine (AZT)	Retrovir®
AZT+3TC	Combivir®
AZT+3TC+ABV	Trizivir®
zalcitabine (ddC)	Hivid®
didanosine (ddI)	Videx®
stavudine (d4T)	Zerit®
<b>NtRTIs (Nucleotide Analog Reverse Transcriptase Inhibitors)</b>	
tenofovir	Viread®
<b>Cellular Factor Inhibitors</b>	
hydroxyurea	Hydrea®

cognitive functions with AZT as well as prevention of HIV infection of the brain. Larger doses (1,000 mg compared to the now-standard 600 mg per day) of AZT appear to be necessary for treating ADC. However, high-dose AZT may present problems since many people with HIV, particularly those who are the sickest, are often unable to tolerate its side effects.

While AZT may be the most researched drug for treating ADC, other anti-HIV drugs that cross the blood-brain barrier may be equally useful. These include AZT, d4T (stavudine, Zerit), abacavir (Ziagen), nevirapine (Viramune), amprenavir (Agenerase) and to a lesser degree indinavir (Crixivan) and 3TC (lamivudine, Epivir). Efavirenz (Sustiva) has not been shown to cross this barrier to a significant degree, but some experts speculate that it may be useful in treating ADC.

Anti-HIV therapies are best used in combinations. It may also be important to consider a drug's ability to cross into the brain when constructing an effective regimen. For

information on developing long-term strategies and creating potent anti-HIV therapy regimen, call Project Inform's Hotline.

## Treating the Symptoms of ADC

Psycho-active drugs are often used to treat the symptoms of ADC. These include anti-psychotics, anti-depressants, anxiolytics, psychostimulants, anti-manics, and anti-convulsants. These drugs do not treat the underlying cause of ADC, or even stop its progression. However, they may ease some of its symptoms. Haloperidol (Haldol) is often used for easing ADC symptoms, though it has many side effects. People with ADC are sensitive to Haldol, so small doses of 5–10mg daily should be used to avoid severe side effects.

Ritalin (methylphenidate) has been used with success in people with ADC to ease apathy and to increase energy, concentration and appetite. Daily doses of 5–10mg are often sufficient.

In cases of severe behavior disorders, anti-psychotics like thiorazine and mellaril can be used to control agitation. Lorazepam (Ativan) and diazepam (Valium) may also be used for sedation and controlling anxiety. Other drugs include perphenazine (Trilafon), thiothixene (Navane), molindole (Moban), and fluoxetine (Prozac) with bupropion (Wellbutrin).



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Many of the therapies listed here may have potential drug interaction with commonly used anti-HIV therapies as well as therapies to treat or prevent HIV-related conditions. For more information about drug interactions, call Project Inform's hotline.

## Conclusion

New treatments for ADC are desperately needed. It's also important that new anti-HIV drugs be fully evaluated for their usefulness in treating ADC. At the same time, promising drugs that may work to treat the underlying causes of ADC also need to be investigated.

This material has been produced as a result of a collaboration between Project Inform and Gay Men's Health Crisis. For more information about Project Inform, call the Project Inform hotline at 1-800-822-7422. For more information about Gay Men's Health Crisis in New York, call 212-367-1451. Special thanks goes to Dr. Richard Price of University of California's San Francisco General Hospital, Neurology Services and Dr. Justin McArthur, Professor of Neurology and Epidemiology at John Hopkin's University in Baltimore for their editorial support.

## What if someone I care for has symptoms or was diagnosed with ADC?

- Help them access the proper diagnosis and treatment.
- Understand that loss of mental and emotional control is terribly frightening for most people, even if it's only moderate or short-term. However, be honest about their symptoms as you offer support and encouragement to establish trust.
- Because mood changes and memory problems are common with ADC, you may encounter resistance while trying to help. Helping the person you care for to write down their symptoms in their own handwriting, as they experience them, can sometimes encourage them to seek medical care.
- Professional caregivers, like home health aides, are sometimes needed to care for people with severe ADC or ADC that doesn't respond to treatment. Seeking this kind of support is sometimes the best way to help those you love.
- Caregiving for someone with memory and behavioral problems can be overwhelming, especially if it's over a long period of time. There are support services in many cities for those who care for others with life-threatening illnesses.

## The Basic Message

- Learn about HIV testing options and choose one that fits your needs! Be sure your privacy is protected!
- If you're positive, don't panic. If you make your health a priority, chances are you will be reasonably healthy for many years.
- Learn about your healthcare options and local support services.
- Get a complete physical and blood tests for CD4+ cell count & HIV level. Repeat quarterly and watch for trends. Women should get GYN exams and Pap tests every six months, more often if abnormal.
- Work with a doctor to develop a long-term strategy for managing HIV disease.
- If the CD4+ cell count is below 350 or falling rapidly, consider starting anti-HIV therapy. Test at least twice before taking action.
- If anti-HIV therapy fails to reduce your HIV level below the "limit of detection" or below 5,000 copies within 3–6 months, consider a different or more aggressive therapy.
- If the CD4+ count trend stays below 300, consider treatment for preventing PCP. If it stays below 200, start treatment for preventing PCP (if you haven't already done so) and reconsider anti-HIV therapy if not on one. Learn about drug interactions and preventive treatments for opportunistic infections.
- If you started preventive therapies and your CD4+ cell count rises in response to anti-HIV therapy, ask your doctor whether it might be safe to stop certain preventive therapies.
- If your CD4+ cell count stays below 75, consider more frequent blood work—perhaps even monthly. Consider therapies for preventing MAC/MAI and CMV.
- Regularly seek support for your personal, spiritual and emotional needs. It takes more than medicines to keep you well.

### HELPFUL READING FROM PROJECT INFORM

Day One; Building a Doctor/Patient Relationship; Making Decisions; and Anti-HIV Therapy Strategies