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I ANTI-HIV AGENTS

A. Switching to nevirapine — results after one year

Background & summary

Highly active antiretroviral therapy (HAART) has improved survival and decreased the chance of death from AIDS-related infections in people who can afford, adhere to, and tolerate the drug cocktails. The last point — tolerate — is important because HAART-users can experience a variety of side effects depending on the combination of drugs taken. One of the more recently recognized side effects is the lipodystrophy syndrome, a term which encompasses the following side effects:

- loss of fat from the face, arms and legs
- extended abdomen and thickening of the waist (“protease paunch”)
- fat pads at the back of the neck (“buffalo hump”) or around the base of the neck (“horse collar”)
- increased breast size
- round, puffy face (“moon face”)
- bulging or visible veins in the arms and/or legs due to the loss of subcutaneous fat (fat under the skin) — fat wasting

In addition to these physical changes, the lipodystrophy syndrome also involves changes in levels of fats and sugar in the blood:

- increased levels of triglycerides (fats)
- decreased levels of high-density lipoprotein (HDL) or “good” cholesterol
- increased levels of low-density lipoprotein (LDL) or “bad” cholesterol
- increased levels of sugar (glucose)
- increased levels of the hormone insulin
- reduced sensitivity to insulin (insulin resistance)

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The precise cause(s) of the lipodystrophy syndrome are not clear. Some doctors suspect that one group of drugs called protease inhibitors (PIs) is responsible for some of the problems with insulin, fat and sugar as well as some of the body shape changes. Other doctors have found that nucleoside analogues (nukes), may play a role in the loss of subcutaneous fat. Some people with HIV/AIDS (PHAs) try to minimize their exposure to PIs by switching to a drug combination based on non-nukes, such as efavirenz (Sustiva) or nevirapine (Viramune), in the hope of reducing their symptoms of lipodystrophy.

Researchers in Spain have been studying the effect of having PHAs switch from a PI-based regimen to one based on nevirapine. According to their results, one year after the switch there were not dramatic reductions in lipodystrophy. However, there were other benefits which we report below.

Study details

Researchers recruited 106 HIV positive adults who had signs/symptoms of lipodystrophy and who had been using a PI-based regimen for at least nine months. Subjects were randomly assigned to receive one of the following regimens:

- nevirapine, ddI (Videx) and d4T (Zerit)
- continued PI-based therapy with at least one PI and two nukes

In addition to regular examinations and lab tests, all subjects received special scans called DEXA (dual-energy X-ray absorptiometry) which was used to assess changes in body composition.

Fifty-two subjects were assigned to receive nevirapine and their profile was as follows:

- 21% female, 79% male
- average age – 36 years
- average CD4+ count – 650 cells
- average CD8+ count – 1,463 cells
- average viral load – fewer than 400 copies
- prior length of PI use – nearly two years

The profile of the 54 subjects who were assigned to receive continued PI-based therapy was as follows:

- 28% female, 72% male
- average age – 41 years
- average CD4+ count – 569 cells
- average CD8+ count – 1,257 cells
- average viral load – fewer than 400 copies
- prior length of PI use – almost two years

On average, researchers monitored subjects for one year.

Side effects — nevirapine

The following side effects developed in the following number of subjects who used nevirapine:

- liver complications – 6 subjects
- painfully swollen pancreas gland (pancreatitis) – 1 subject
- severe rash – 3 subjects

All subjects who developed liver damage while using nevirapine were co-infected with hepatitis C virus (HCV). Interestingly, five out of six subjects who developed this complication were women. A total of six subjects had to stop using nevirapine — two because of rash and four because of liver damage.

Side effects — PI regimens

The following side effects developed in the following number of subjects who used PI-based regimens:

- kidney stones – 3 subjects; this was caused by indinavir (Crixivan)
- diarrhea (more than three bowel movements daily) – 3 subjects

Nine subjects in the PI group stopped using their anti-HIV medications for the following reasons:

- “self-perceived” worsening of lipodystrophy – 2 subjects
- indinavir-related kidney stones – 3 subjects
- severe diarrhea – 3 subjects
- nerve damage – 1 subject

Changes in viral load

The following number of subjects in each group had their viral load rise above the 400 copy mark while in the study:

- nevirapine group – 5 subjects
- PI group – 3 subjects

These increases in viral load were likely due to HIV becoming resistant to the treatments used by these subjects. The researchers noted that all of the eight subjects had used “multiple” nukes before entering the study, so the likelihood of developing drug-resistance was high. These results are worth bearing in mind by doctors who wish to consider prescribing simpler drug regimens.

By the end of the study, the following proportion of subjects in each group had achieved a viral load below the 50 copy mark:

- nevirapine group – 74%
- PI group – 72%

This difference was not statistically significant.

Changes in cell counts

On average, in each group, there was the following increase in CD4+ cell counts by the end of the study:

- nevirapine group – 112 extra cells
- PI group – 163 extra cells

There were also increased levels of CD8+ cells, with each group having the following number of extra CD8+ cells by the end of the study:

- nevirapine group – 256 cells
- PI group – 163 cells

Again, these differences between the two groups were not statistically significant.

Changes in body shape

DEXA scans did not detect any major changes in body composition, although subjects who switched from PI-based regimens to nevirapine did tend to experience a decrease in subcutaneous fat.

Lipid levels

Among subjects who switched from PIs to nevirapine, a significant decrease in cholesterol and triglyceride levels occurred by the end of the study. No significant changes occurred in this regard among the subjects who continued to use PI-based regimens.

Quality of life

According to the researchers, subjects using nevirapine reported significantly better quality of life than subjects using PIs, mainly because drug regimens became simpler — fewer pills, easier dosage schedules — once subjects switched to nevirapine. Other improvements occurred because side effects from PIs were no longer present. All of these improvements continued to the end of the study.

Another look at lipo

The researchers noticed that those PHAs who were experiencing fat wasting before entering the study continued to do so regardless of which study regimen they were assigned. It may be that longer periods — more than one year — are required for PHAs to recover from lipodystrophy. It is also possible that continued use of nukes contributes to fat wasting.

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B. Effect of HAART on cervical growths

Background

The use of highly active antiretroviral therapy (HAART) has greatly improved survival rates among people with HIV/AIDS (PHAs). This occurs because HAART suppresses production of HIV, which allows the immune system to begin repairing itself. Unfortunately, the immune system does not become fully restored, perhaps because a low level of viral activity occurs even though HAART is used. As a result, the immune system is not 100% effective and some complications can still occur. This means that although the level of restored immunity may be enough to help PHAs resist many AIDS-related infections, it does not appear to be sufficient to prevent the development of some cancers.

HPV

A virus called HPV (human papilloma virus) causes cervical and anal lesions and, in some cases, those lesions can turn into tumours. Because of their weakened immune systems, PHAs co-infected with HIV and HPV are at increased risk for HPV-related cancers. In the time before HAART, one study found that HIV positive women were five times more likely than HIV negative women to develop abnormal growths on the cervix.

To understand the impact of HAART on HPV infection and cervical growth, researchers in Milan, Italy, recruited 163 HIV positive women between 1995 and 1997 and monitored their health. The average age of the women was 34 years. Researchers divided the women into three groups based on their use of anti-HIV therapy. Their profile at the start of the study was as follows:

Group 1 – no therapy

- 27 subjects
- average CD4+ count – 627 cells
- average viral load – 1,100 copies

Group 2 – one or two nucleoside analogues (nukes)

- 62 subjects
- average CD4+ count – 336 cells
- average viral load – 288 copies

Group 3 – HAART

- 74 subjects
- average CD4+ count – 260 cells
- average viral load – 1,200 copies

All subjects received regular Pap smears along with gynecologic exams. Abnormal growths were removed for analysis. Those women who had pre-cancerous cervical lesions had them zapped with a mild electric

current. On average, researchers monitored subjects for about 1½ years.

Results — Types of HPV

There are many strains of HPV, only some of which — such as HPV-16, HPV-18, HPV-31 and HPV-33 — are considered to place women at high risk for developing pre-cancerous cervical growths. Researchers found that only 65% of the women had detectable HPV. In these women, the following proportion had the following types of HPV:

- 33% – HPV-31, -33, -35 or -45
- 25% – HPV-16
- 2% – HPV-18
- 25% – many types of HPV
- 16% – had detectable HPV but technicians were unable to tell which type

Results — Pap smears

At the start of the study, results of Pap smears were as follows:

- normal – 73% of subjects
- abnormal cells detected – 20%
- pre-cancerous cells detected – 6%

In general, women with low CD4+ cell counts were more likely to have cervical growths than women with higher cell counts. The proportion of women who had pre-cancerous growths in different CD4+ cell count ranges were as follows:

- more than 500 CD4+ cells – 3% had pre-cancerous growths
- between 200 and 500 CD4+ cells – 5% had precancerous growths
- fewer than 200 CD4+ cells – 6% had pre-cancerous growths

Not surprisingly, the researchers observed that only those women who used HAART had significantly increased CD4+ cell counts during the study.

A total of 53 women had colposcopies during which abnormal cervical growths were removed for analysis. Pre-cancerous cells were detected in only seven of these 53 women.

According to the data analysis, the researchers found the following:

- Neither treatment with nukes alone nor HAART significantly reduced the risk of having abnormal

cervical growths develop into the pre-cancerous stage.

- Women who had fewer than 350 CD4+ cells by the end of study were significantly more likely to have persistent infection with HPV-16 or HPV-18.
- Subjects who received HAART were significantly less likely than other subjects to have detectable HPV-16 or HPV-18.

Despite the findings above, pre-cancerous cervical growths were not more likely to shrink in women receiving HAART or nukes alone compared to women receiving no anti-HIV treatment.

During the study, no cases of invasive cervical cancer were detected. The researchers did point out that two women using HAART who were not in the study but who sought medical care from their clinic while the study was ongoing, did develop this form of cancer. This anecdote underscores the fact that cervical cancer can occur in women using HAART.

The results of this study suggest that despite the use of HAART, HPV cervical infection and related disease continue in women who receive HAART. The study doctors emphasize the need for HIV positive women to receive regular gynecologic monitoring as part of their overall care.

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II IMMUNE BOOSTERS

A. Immune booster used to fight drug-resistant herpes

Infection with herpes viruses can cause sores and, in some cases, ulcers in the mouths and genitals of people. These sores can usually be treated with the following drugs:

- acyclovir (Zovirax)
- Valtrex (valacyclovir)
- Famvir (famciclovir)

Unfortunately, cases of herpes that are resistant to these drugs are increasingly leaving doctors and their patients with few options. However, a group of doctors in New York recently reported the case of a person with AIDS who successfully recovered from drug-resistant herpes when he was treated with the immune booster Aldara (imiquimod).

Details

The doctors provided details on a 34-year-old man whose CD4+ count was 200 cells and whose viral load was “undetectable.” He had been taking highly active antiretroviral therapy (HAART) for about a year and had symptoms of herpes on his genitals for about five months. Doctors prescribed the following regimens one at a time to treat the herpes infection:

- acyclovir – 1,200 mg/day for one month
- Valtrex – 2 grams/day for one month
- Famvir – 1,500 mg/day for one month

Because these drugs did not help, doctors then prescribed 5% Aldara cream, which the man applied to his lesions and then washed off eight hours later. He did this three times in one week and then stopped the drug.

Results

After four days, the pain from the herpes infection cleared. After one week, the lesions healed. The man has remained free from herpes lesions for at least one month and did not report any side effects associated with Aldara.

Aldara is licensed in North America for the treatment of warts on the genitals and anus. This drug appears to work by stimulating CD8+ cells and other cells of the immune system in the skin to fight viral infections. The drug is currently being investigated for the treatment of certain types of skin cancer. It has also been used to treat another troublesome

AIDS-related complication — mollusca lesions — caused by MCV (*Mollusca contagiosum* virus). Further research on Aldara, and possibly more effective immune boosters such as resiquimod, is underway.

Aldara is not for everyone. The drug can cause severe skin irritation, rash and itching, among other side effects. Doctors are not sure if the drug will work for people with HIV/AIDS who have very low CD4+ counts. The team of doctors in New York suggests that Aldara be tested in clinical trials to confirm its anti-herpes activity.

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III SIDE EFFECTS

A. Sexual dysfunction and HAART

Background & summary

The use of highly active antiretroviral therapy (HAART) can cause many side effects, as mentioned in our report on nevirapine. One possible side effect of HAART that is not usually mentioned is sexual dysfunction. There's not much information on this problem, in part because people in clinical trials of HIV/AIDS drugs are not usually questioned about sexual dysfunction. As well, both research subjects

and data collectors may not feel comfortable talking about this issue.

To help find out more about sexual dysfunction, researchers in the European Union surveyed over 900 people with HIV/AIDS (PHAs). According to their results, a large proportion of PHAs, particularly those using protease-inhibitors (PIs), reported sexual dysfunction. These results are interesting but there are some important points to consider about this study before assuming that PIs cause sexual dysfunction.

Study details

Researchers distributed surveys between 1998 and 1999 at eight major HIV/AIDS treatment centres and four non-governmental organizations in the European Union. The profile of the 904 subjects whose data was used in the analysis was as follows:

- 20% female, 80% male
- average age – 39 years
- time since diagnosis of HIV – 8 years

The proportion of subjects with the following CD4+ cells counts was:

- more than 500 CD4+ cells – 29%
- between 200 to 500 CD4+ cells – 49%
- fewer than 200 CD4+ cells – 22%

The proportion of subjects with the following range of viral loads was:

- fewer than 500 copies – 43%
- between 500 to 30,000 copies – 43%
- more than 30,000 copies – 14%

The proportion of subjects with symptoms of HIV/AIDS was as follows:

- symptom-free – 55%
- mild symptoms – 30%
- symptoms of AIDS – 15%

The following therapies were used by the following proportion of subjects:

- PI-based regimens – 75%
- nucleoside analogues (nukes) only – 10%
- combinations of nukes and non-nukes – 13%

Results — Sexual dysfunction

The researchers found that about 37% of their subjects (29% female, 38% male) reported decreased interest in sex. Other findings included:

- 31% of males reported decreased “sexual potency”

- decreased sexual interest was more likely to occur among PI-users (40%) compared to subjects not using these drugs (16%)

Among those subjects who used PIs, decreased sexual interest occurred more often among those who had signs/symptoms of lipodystrophy (49%) than in those PI-users who did not have lipodystrophy (25%). As well, those subjects who had another complication — nerve damage to the hands and/or feet (peripheral neuropathy) — were also likely to have reduced sexual interest.

The following factors were linked to decreased sexual potency:

- having symptoms of HIV/AIDS
- use of tranquillizers
- use of antidepressants
- use of indinavir (Crixivan) or ritonavir (Norvir)

In general, the researchers found that as the age of subjects increased, so did the risk of sexual dysfunction.

Points to consider

1. Before rushing to blame PIs for yet another side effect, it is important to remember that sexual dysfunction can be caused by several factors, including depression. Researchers did not enquire about this problem, which makes interpreting the results of their survey difficult.

2. The finding about indinavir and ritonavir — but not nelfinavir — being linked to sexual dysfunction is interesting. This does not mean that nelfinavir cannot be associated with sexual dysfunction. The problem in this study was that the average length of time subjects used nelfinavir was shorter than the length of time they used indinavir and ritonavir. Results might have been different if researchers had used subjects who had taken different PIs for the same length of time.

3. Researchers need to design and conduct better studies if they are to be certain about the link between something as complex as sexual interest and the use of certain HIV drugs. They also need to rule out other conditions that can cause sexual dysfunction, such as cardiovascular disease, lower-than-normal concentrations of testosterone/estrogen, depression, and use of substances and other medications such as lipid-lowering agents.

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B. Lipid-lowering drugs and changes to diet can make a difference

Background & summary

Increased levels of lipids or fatty substances — triglycerides and cholesterol — in the blood of some people with HIV/AIDS (PHAs) who use highly active antiretroviral therapy (HAART) places them at increased risk for cardiovascular disease.

Aware of the risk posed by the increase in lipid levels, doctors who treat HAART-users have prescribed lipid-lowering drugs commonly called statins, examples of which include the following:

- Crestor (rosuvastatin)
- Lescol (fluvastatin)
- Lipitor (atorvastatin)
- NK-104 (pitavastatin)
- Mevacor (lovastatin)
- Pravachol (pravastatin)
- Zocor (simvastatin)

In HIV negative people, these drugs have helped to reduce the risk of heart disease. It is not clear which statin is best for PHAs. The answer to this question may well be different for each PHA and may depend on a number of factors, including which treatment regimen a PHA is taking. This is because statins, like protease inhibitors (PIs) and non-nukes, are processed by enzymes in the liver. Using a statin with a PI and/or non-nuke that is processed by the same liver enzyme(s) can affect the activity of those enzymes, meaning that there is the potential for these drugs to interact. Such an interaction could raise or lower levels of one or both drugs in the blood. This can weaken the activity of anti-HIV drugs, leading to resistance, or it could cause new side effects or enhance pre-existing side effects.

Researchers in London, England, conducted a six-month study in 31 male subjects who were receiving PI-based treatment and who had higher-than-normal levels of cholesterol. Half the subjects received advice

about changing their diet (dietary advice). The other half received the same advice along with the lipid-lowering drug Pravachol (pravastatin), 40 mg per day. By the end of the study, cholesterol levels fell in the Pravachol-users by 17% and in those receiving dietary advice alone, by 4%.

Study details

Researchers recruited 31 male subjects who were receiving the following PIs as part of their treatment regimen:

- ritonavir (Norvir) with saquinavir (Fortovase) – 9 subjects
- indinavir (Crixivan) – 9 subjects
- nelfinavir (Viracept) – 6 subjects
- indinavir with ritonavir – 3 subjects
- ritonavir – 2 subjects
- nelfinavir with saquinavir – 1 subject

All subjects received advice about reducing their intake of cholesterol-rich food. They were also advised to quit smoking and begin a programme of regular exercise. Subjects were randomly assigned to receive dietary advice alone or dietary advice with Pravachol 40 mg per day. The drug was taken at a dose of 20 mg per day for the first two weeks after which the dose was increased to 40 mg per day.

At the start of the study, the basic profile of subjects in each group was as follows:

Dietary advice alone —

- average cholesterol – 7.4 mmol/Litre
- average triglyceride – 4.06 mmol/Litre
- average CD4+ count – 290 cells
- average viral load – fewer than 500 copies

Dietary advice and Pravachol —

- average cholesterol – 7.5 mmol/Litre
- average triglycerides – 3.96 mmol/Litre
- average CD4+ count – 407 cells
- average viral load – fewer than 500 copies

Results — Changes in cholesterol levels

Five subjects left the study for “personal reasons,” four of whom were in the dietary advice group and one in the advice and statin group. On average, cholesterol levels fell by the following proportion in each of the following groups:

- dietary advice only – 17.3%
- Pravachol – 4%

This difference between the two groups was almost statistically significant. No significant changes to triglyceride levels occurred during the study.

Side effects

Although statins are supposed to be well-tolerated drugs, they can cause tiredness in some users. More seriously, they can damage muscles, causing muscle pain and weakness. No subjects in this study developed such problems. As well, there were no reports of liver damage due to use of Pravachol.

Changes to the diet

Dietary advice apparently had a greater impact in those subjects who received this advice without a statin. For instance, the intake of saturated fat (generally fat of animal origin) fell by 38% in the group receiving advice only but rose by 2% in the group receiving Pravachol. Intake of sugar fell by 50% in the group receiving dietary advice only and only by 8% in the advice and Pravachol group.

The changes in lipid levels seen in this six-month study, particularly among Pravachol-users, are not surprising. Perhaps more significant changes may have occurred among these subjects had they adhered to suggested changes in diet and exercise. Readers should note that it may be more difficult to reduce lipid levels in people using HAART than in HIV negative people not taking HAART. Other interventions such as eating fish that is rich in omega-3 fatty acids — cod, haddock, herring, tuna, salmon and sardines — as well as the use of supplements such as L-carnitine and antioxidants need to be tested in HAART-users with high lipid levels in their blood.

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C. Carnitine for high triglycerides

Carnitine is an amino acid that is used to help move fatty substances to places inside cells where they can be burnt to release energy. The parts of a cell where this energy release takes place are called mitochondria. Carnitine can also act as an antioxidant and appears to play a role in maintaining the health of nerves and protecting the liver and kidneys from the toxicity of drugs. Carnitine exists in several forms; the two most commonly used are L-carnitine and L-acetyl-carnitine.

A number of studies have found that people with HIV/AIDS (PHAs) may have less-than-normal levels of carnitine. Signs/symptoms of carnitine deficiency include the following:

- higher-than-normal levels of triglycerides

- weak and/or tired muscles

As some PHAs can develop high triglyceride (TG) levels in their blood — whether or not they are taking anti-HIV drugs — research teams in Montreal and Rome have found that supplements of this nutrient may be helpful for PHAs. The Montreal team recently conducted a small study to observe the effect of carnitine supplements on high TG levels in people with HIV.

Study details

Researchers enrolled 16 adult subjects who had the following profile at the start of the study:

- 1 female, 15 male
- average age – 43 years
- all but one were using protease inhibitors
- average viral load – 2,500 copies
- average CD4+ count – 218 cells
- average TG level – 5.67 mmol/Litre (normal range 0.5 to 2.0)
- average cholesterol – 5.6 mmol/Litre (normal range 2 to 5.2)
- average glucose – 5.3 mmol/Litre (normal range 3.6 to 6.1)

Subjects received 3 grams of L-carnitine daily for an average of nine months.

Results

One month after entering the study TG levels had decreased by an average of 39% — a significant decrease from their pre-study levels. This decrease was maintained throughout the study.

According to the researchers, “near-normal TG levels (3 mmol/Litre or lower)” were seen in 54% of subjects after two months of L-carnitine use, and in 69% of subjects after their last lab test. There were no significant changes in cholesterol or glucose levels during the study.

No serious side effects from L-carnitine were reported and, at a dose of 3 grams per day, L-carnitine appears to be relatively safe. The results of this pilot study will be used to plan a larger, more complex trial. Carnitine is sold in North America as the prescription drug Carnitor. L-carnitine and L-acetyl-carnitine are also available from some health food stores, particularly in the United States.

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IV NERVES

A. Depression linked to immune system decline in women

Background & summary

Some studies have found that depression among men with HIV speeds up the decline of their immune system. Little research has been done on the impact of depressive illness on the health of women with HIV/AIDS. Studies have found that between 30% to 60% of HIV positive women tend to experience depression, while in HIV positive men the figure is around 20%.

Earlier this year, researchers at Yale University and elsewhere in the U.S. published results from a study on more than 700 HIV positive women whom they monitored for up to seven years. The researchers found that those women who had prolonged episodes of depression were twice as likely to die than women who had mild or no symptoms of depression.

Study details

Researchers reported results on 765 HIV positive women who made regular visits to study clinics so that their health could be assessed. Researchers began recruitment between 1993 and 1995. Monitoring continued until March 2000. Thus, in some cases, researchers collected up to seven years of data. Subjects had the following profile at the start of the study:

- average age – 34 years
- average CD4+ cell count – 427 cells
- average viral load – 10,428 copies
- 46% were free from symptoms of HIV/AIDS
- 42% had one or two symptoms
- 11% had three or more symptoms

During the study the following drugs were used by the proportion of women indicated:

- more than one year of HAART – 38%
- less than one year of HAART – 42%
- two or more anti-HIV drugs – 20%
- one anti-HIV drug – 12%
- no therapy – 18%

During the study, subjects admitted to the following activities with the drugs listed:

- inhaling cocaine – 19%
- injecting narcotics – 15%
- using both types of drugs – 12%

Most women in the study (54%) denied using any of the above drugs.

During the study, the following degrees of depression affected the proportion of women indicated:

- chronic (continuous) depression – 42%
- intermittent (from time to time) depression – 35%
- limited or no symptoms of depression – 23%

Results — Effect of depression on survival

During the study 14% (106) of the women died from HIV-related causes (these were not specified by the researchers). Within each type of depression, the following proportion of women died:

- chronic depression – 23%
- intermittent depression – 16%
- limited or no symptoms of depression – 8%

The differences between the three groups were statistically significant, that is, not likely due to chance alone.

Age and employment

The researchers also found that subjects who were 35 years or older were 1.5 times more likely to die than younger subjects. As well, women who were unemployed were twice as likely to die compared to those who were employed.

Depression and CD4+ cells

Researchers matched categories of depression and CD4+ counts to find out the impact of each on the survival of women in the study.

Among women who had fewer than 200 CD4+ cells and the following categories of depression, the proportion who died was as follows:

- chronic depression – 54%
 - intermittent symptoms of depression – 48%
 - limited or no symptoms of depression – 21%
-

These differences were statistically significant.

Among women who had between 200 and 500 CD4+ cells and the following categories of depression, the proportion who died was as follows:

- chronic depression – 16%
- intermittent depression – 11%
- limited or no depression – 7%

These differences in death rates were not significant although there is a trend for an increased risk of death as depression becomes more serious.

Among women who had more than 500 CD4+ cells there was no significant difference in death rates for the three categories of depression.

Depression and declining CD4+ cell counts

The researchers noted that those subjects who had chronic or intermittent depression had a larger decline in CD4+ counts over the course of the study compared with women who had only a limited number or no symptoms of depression. This difference was statistically significant.

Women with the following profile in the study also had a relatively high loss of CD4+ cells:

- use of HAART for less than one year
- not using HAART
- who were black
- low-income
- unemployed
- receiving welfare
- did not graduate from high school

Just as depression influenced the loss of CD4+ cells, it also affected the amount of virus in the blood — viral load. Women with chronic depression were more likely to have higher viral loads than women with few or no symptoms of depression.

Linking depression to other problems

According to the researchers, “Determining a clear cause-and-effect relationship between depression and HIV disease progression is complex because symptoms for both conditions overlap.”

Nonetheless, the researchers suggested that depressive illness “contributes uniquely [to death and is not simply a result] of declining health.”

Depression may indirectly influence health by changing levels of hormones in the brain, which weaken the immune system and directly weaken

immunity through contact between a depressed brain and cells of the immune system.

Depression can also cause problems in other ways:

- increasing the likelihood of alcohol and other drug abuse
- decreasing interest in sleep, eating and other basic health-maintaining behaviours
- decreasing adherence to medication
- decreasing the will to live

The results of this study should highlight the importance of depression in HIV positive women to health care providers so that they can identify women at risk for depression, monitor them and offer them treatment or therapy for this condition. In the research field, more work needs to be done to develop novel antidepressants that work faster and have fewer side effects and drug interactions than currently licensed therapies. And, last but not least, women with HIV and their family members need to be educated about depression and its symptoms.

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Disclaimer

Decisions about particular medical treatments should *always* be made in consultation with a qualified medical practitioner knowledgeable about HIV-related illness and the treatments in question.

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