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I SIDE EFFECTS AND COMPLICATIONS

A. Study finds heart disease in young HIV-positive men

The widespread availability of potent anti-HIV therapy has prolonged the survival of HIV-positive people, particularly those who live in high-income countries and who are engaged in their care and treatment. However, anti-HIV therapy does not cure HIV infection and increased survival is accompanied by other problems, most notably an apparent acceleration of the aging process that affects many organ-systems.

How might prolonged HIV infection accelerate the aging process? Researchers are not certain but have begun to study the interaction between HIV and aging. One possible way prolonged HIV infection might cause damage to the body is through chronic immune activation. Shortly after encountering HIV, the immune system goes into an activated state as it tries to contain this infection. Unfortunately, HIV can evade the body's defenses, and once infection becomes chronic a lifelong fight between the immune system and HIV ensues. This prolonged struggle between the immune system and HIV ensures that the cells of the immune system are often in an activated state. Furthermore, the heart and blood vessels are particularly vulnerable to damage arising from immune activation.

Therapy for HIV greatly suppresses levels of this virus. With reduced levels of HIV, the immune system does attempt to turn off its activation. However, this is not completely successful. The immune system communicates with and can affect other organ-systems. Indeed, some of the immune system's cells even take up residence in organ-systems. There, they release chemical messengers

produced by



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that can inflame tissue; over time, this inflammation can lead to damage.

Researchers at Harvard University have been studying the impact of HIV on the blood vessels of HIV-positive men. Their findings suggest that in relatively young, symptom-free men, HIV infection can cause a narrowing of the arteries, increasing the risk for a heart attack.

Study details

Researchers recruited 110 men who were divided into two groups as follows:

- HIV positive – 78 men
- HIV negative – 32 men

The data from HIV-negative men were used for purposes of comparison and our report will focus on HIV-positive men.

All men in the study were symptom-free and at the time of recruitment were not known to have cardiovascular disease (CVD).

Participants were interviewed, examined and had CAT scans of their heart performed. In addition, a cardiologist performed coronary angiography—a procedure to assess blood flow in the vessels that supply oxygen-rich blood to the heart.

The average profile of HIV-positive participants was as follows:

- age – 47 years
- 35% were tobacco smokers
- 29% had high blood pressure
- 9% had diabetes
- length of time with HIV – 14 years
- CD4+ count – 523 cells
- 81% had a viral load below the 50-copy mark
- 95% were taking anti-HIV therapy

Of the four men who were not taking anti-HIV therapy, their CD4+ counts were about 800 cells and viral load just over 1,000 copies.

Results—Looking for heart disease the usual way

Analysis of information gathered from blood samples, physical examinations and interviews found that factors such as age, race, diet and weight were similar between the two groups. Results from most blood tests regarding cholesterol and sugar were also broadly similar. Based on these results, the men would have been

considered at low risk (about 5%) for having a heart attack in the next 10 years.

Results—CAT scans

Although the results of traditional assessments of CVD seemed reassuring, when researchers analysed the findings from CAT scans and angiography they found that nearly 60% of the HIV-positive men had sticky deposits on the walls of their arteries. These deposits are called plaque and are made up of cholesterol, debris and sometimes calcium; they also can contain cells of the immune system that are attracted to plaque because of inflammation. Large plaques can clog arteries and choke the flow of blood and oxygen to the heart, which can lead to a heart attack. Sometimes plaques can rupture and trigger the formation of blood clots that block the flow of blood, leading to heart attacks and, if the clots reach the brain, stroke. In contrast, among the HIV-negative men, only 34% had plaques in their arteries. This difference was statistically significant.

Narrowed arteries

The researchers also found that in about 7% of HIV-positive men there was a great deal of blockage in the arteries that supply oxygen and nutrients to the heart—the coronary arteries. In 7% of HIV-positive men, at least 70% of blood was blocked from flowing through to the heart. This blockage increased their 10-year risk of a heart attack from 5% to 12%. In contrast, among HIV-negative men with a significant narrowing of the arteries, their 10-year risk of a heart attack was about 4%—a significant difference.

To the clinic

In five HIV-positive men who had significantly narrowed arteries, the researchers informed their family doctors and asked them to refer the men to a cardiologist. Here is what happened:

- One man underwent a cardiac stress test and had a normal result and is so far doing well.
- Another man is awaiting his cardiac stress test.

The remaining three men were evaluated by cardiologists who conducted further testing, which confirmed that they had severely narrowed arteries. One of the three underwent coronary bypass surgery; another had a stent placed inside his artery to keep it open. In the case of the fifth man, doctors tried to implant a stent but failed. They also prescribed cholesterol-lowering medicines but the man was unable to tolerate them. Two years later, investigation revealed that his arteries had

narrowed even more and so he received bypass surgery. All three people are “doing well,” according to the research team.

Zeroing in on narrowed arteries

The study team found that HIV-positive men with plaque in their arteries were likely to have the following features:

- older age
- HIV infection for a longer period of time
- higher total cholesterol, triglycerides and bad cholesterol (LDL-C)
- low ratio of CD4 to CD8 cells
- elevated levels of a chemical messenger used by the immune system called MCP-1 (monocyte chemoattractant protein-1)

Although some observational studies have linked exposure to anti-HIV drugs to an increased risk for CVD, the Harvard study did not. However, the researchers did find that men who had high levels of antibodies to a virus called CMV (cytomegalovirus) were more likely to have evidence of heart disease.

The burden of plaque

Taking many factors into account—including age, use of protease inhibitors, cholesterol levels, viral load, CD4+ cell count—the researchers found that the longer a person had been HIV positive, the greater the likelihood that they had extensive and thick deposits of plaque.

Caution on calcium score

Calcium can sometimes be deposited in plaque. Some studies of plaque have focused only on finding calcium-containing plaque and linking these to an increased risk for CVD. These studies produce a calcium score to indicate the level of calcium in arteries. However, plaques may be present without detectable calcium deposits. The Harvard team noted that in their study “a significant proportion of patients with coronary atherosclerosis would have been missed if calcium score was used as the sole [way to assess] coronary atherosclerosis.”

Understanding the link

The findings from the Harvard study suggest that there is a link between HIV infection and narrowed arteries that is independent of traditional CVD risk factors. This link appears to be related to the length of time a person has been HIV positive. HIV plays a role in CVD, perhaps by triggering or intensifying inflammation.

The immune system

That the CD4/CD8 ratio was linked to CVD suggests that the immune system may also play a role in this problem. Another clue comes from the finding that higher levels of the immune system chemical messenger MCP-1 were found in men at high risk for CVD. MCP-1 attracts a group of cells called monocytes. Monocytes, and their mature form called macrophages, are found throughout the body. Previous research has found that MCP-1 is an important signal that attracts monocytes to plaques in arteries. HIV-infected cells release proteins that also stimulate the release of MCP-1. And other researchers have found that MCP-1 is linked to an increased risk of CVD in both HIV-negative and HIV-positive people.

CMV

Cytomegalovirus, or CMV, is a member of the herpes family of viruses. In immune-suppressed people with low CD4+ counts, CMV infection can cause ulcers and damage the light-sensitive portion of the eye, leading to blindness. Some researchers have a theory that CMV infection is linked to an increased risk for CVD. Data for this theory arises from research in mice that shows that CMV infection can raise blood pressure and perhaps cause other complications. Studies of large numbers of people have found an association between having CMV infection and CVD. However, more research needs to be done in people to understand the possible role played by CMV as a risk factor for CVD in HIV-positive people.

In the future

The Harvard study focused only on men. Additional studies are needed to monitor CVD health in both HIV-positive men and women over time to see if the present study’s findings change. Important questions such as the following need to be answered:

- How fast does CVD get worse because of HIV?
- What is the most effective therapy to help HIV-positive people quit smoking?
- Changes to eating habits, such as the increasingly studied DASH (dietary approaches to stop hypertension) diet, can have a dramatic impact on CVD risk in HIV-negative people. Is the DASH diet similarly safe and effective in HIV-positive people?
- What role do anti-inflammatory medicines (such as Aspirin and statins) and supplements (such as fish oil) have in HIV infection and CVD risk?

- Will earlier use of anti-HIV therapy reduce the speed at which CVD develops?

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B. DAD: an updated analysis of heart attack risk

Some HIV-positive people can have more traditional risk factors for cardiovascular disease than HIV-negative people, including one or more of the following:

- smoking tobacco
- abnormal cholesterol levels
- injecting illicit drugs such as cocaine, crystal meth or heroin

A large database called DAD has collected health information on just over 33,000 HIV-positive people living on several continents. DAD regularly analyses its data to find associations between the medicines people take and possible side effects.

The latest report from DAD focuses on the association between heart attacks and the use of particular anti-HIV drugs.

Understanding risk

Before discussing the latest analysis from the DAD study, it might be helpful to review how researchers talk about risk.

Normally, when we speak about risk, we mean overall (or absolute) risk, which tells us the probability that a certain event (such as a heart attack) will happen over a given period of time. Generally speaking, the overall risk of a heart attack in people living with HIV is quite low. Overall, about 2% of 33,000 people in the DAD study developed a heart attack; so in the DAD study, heart attacks are generally uncommon. However, everyone's overall risk for a heart attack is different, so some people living with HIV may have a much higher overall risk depending on risk factors such as whether or not they smoke or their family history of heart attack.

When researchers want to study the risk of a heart attack associated with taking a particular drug, they try to measure the *percentage change* in the overall risk that results from taking that drug. This is called the relative risk. The relative risk gives us information about how much more (or less) likely a heart attack will be if the person is taking the particular drug studied compared to if they are not taking the drug. For example, a study may find a 70% increase in the relative risk of a heart attack. This means that the risk of a heart attack is 70% higher among people taking the drug than among people who are not taking the drug. The relative risk measures a change in risk, it does not measure the overall risk

In order to know what the relative risk, reported by researchers, means for you, you need to also consider your overall risk for heart attack. Your doctor can help you to determine your overall risk. If your overall risk of a heart attack is low prior to starting the drug, a 70% increased relative risk might not be significant compared to someone else whose initial overall risk for a heart attack is very high. And bear in mind that a 70% increase in relative risk does NOT mean that there is a 70% chance you will get a heart attack.

Now, onto the DAD study.

Study details

The DAD study group analysed data from 33,308 HIV-positive people and divided them into two groups as follows;

- 580 people who had a definite or possible heart attack
- 32,728 people who did not have a heart attack

Results—Profile of people with a heart attack

In general, people who experienced a heart attack, compared to people who did not, were more likely to have the following features:

- male
- age – 50 years and older
- have a personal or family history of cardiovascular disease (CVD)
- diabetes
- high blood pressure
- abnormal lipid levels
- be at high risk for CVD

Heart attack risk—protease inhibitors

DAD found that the relative *risk* of a heart attack increased with each year that the following drugs were used:

- indinavir (Crixivan) – 12% increased relative risk for a heart attack each year
- lopinavir-ritonavir (Kaletra) – 13% increased relative risk for a heart attack each year

Both indinavir and lopinavir-ritonavir belong to the family or class of anti-HIV drugs called protease inhibitors. So far, no other protease inhibitors have been associated with an increased relative risk for heart attack in the DAD study.

Heart attack risk—nukes

Abacavir (Ziagen, and in Kivexa and Trizivir) and ddI (Videx EC) belong to a group of drugs called nukes (nucleoside analogues). For each year that a person took abacavir, DAD found that their relative risk of a heart attack increased by 7%. This risk is relatively small and has been described by expert reviewers as “marginal.” However, among people who were either currently using or had used abacavir within the past six months, the relative risk of a heart attack increased 70%.

Among people who used ddI recently, there was a 41% increased relative risk for a heart attack.

Why is caution needed?

The DAD study design is that of an observational or cohort study. Such studies are very good at finding associations—in this case, between the use of a certain drug and having a heart attack. However, observational studies by their nature can only find associations; they cannot prove cause and effect. That is, they cannot prove that taking a particular medicine(s) will indeed cause a particular effect (heart attack).

Furthermore, confounding or channeling bias is a problem that bedevils observational studies and makes drawing firm conclusions difficult when interpreting the data. Observational studies are useful for finding associations that can later be explored in studies of a more robust design, such as a randomized clinical trial.

Kidney disease increases the risk for a heart attack, as a report later in this issue of *TreatmentUpdate* notes. However, the DAD researchers can only account for some cases of kidney disease and its impact on cardiovascular health. The issue of kidney disease and its impact on CVD health in DAD needs to be investigated further.

Substance use

Taking stimulants such as cocaine, crystal meth and ecstasy can greatly stress the heart and blood vessels, increasing the risk for a heart attack. Also, people who inject drugs are prone to bacterial infections that attack the heart. Another large database, the French Hospital Database (FHDB), found that people who injected illicit drugs **and** who used abacavir were at heightened risk for a heart attack.

DAD needs to assess substance use in its records and find out if there was a link to heart attacks.

Changing findings

DAD has previously reported that exposure to all protease inhibitors was associated with a 16% increased relative risk of heart attack for each year that these drugs were used. Now, DAD has taken into account exposure to nukes and found that only two protease inhibitors—indinavir and lopinavir-ritonavir—are associated with this problem.

Also, DAD previously found that the relative risk of a heart attack when using abacavir was increased by about 90%. In the present analysis the relative risk has declined but is still high, at 70%.

There may be further changes to DAD’s analyses in the years ahead.

Guiding the reader

Biomedical journals sometimes publish editorials or commentaries to help readers make sense of complex research studies. To accompany the latest report from DAD, the *Journal of Infectious Diseases* published an editorial that noted the limitations of

observational studies. The editorial, in reflecting on how DAD did its data analysis stated:

“It could be easy to be misled by apparent induced associations.”

The DAD team is aware of the study’s limitations and has conducted sensitivity analyses to check for hidden biases that may occur when interpreting the data. But the editorial in the *Journal of Infectious Diseases* notes this about sensitivity analyses:

“Such analyses may induce or attenuate associations between treatment and outcome.”

One of the issues with the association found in DAD between abacavir and heart attacks is this: Two years since the first report by DAD, there is no conclusive evidence of how abacavir might increase the risk for a heart attack. An important point to bear in mind is that the proportion of people who had a heart attack in DAD is very low—about 2%.

What to do?

Committees of physicians and researchers who help write treatment guidelines in the European Union and the United States are aware of DAD’s strengths and weaknesses and have offered this advice about abacavir and heart attacks:

“Abacavir should be used cautiously in people at high risk for cardiovascular disease.”

Since HIV infection is associated with an apparent accelerated aging of the cardiovascular system, more attention needs to be paid to reducing or ideally eliminating modifiable risk factors for a heart attack.

For more ways to have a healthy heart, see CATIE’s in-depth Fact Sheet available here:

www.catie.ca/facts.nsf/9a83231f2055bda9852566b90004b064/78ab93dc461831ea85257680006d5d24!OpenDocument

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C. High risk of heart problems in people with kidney dysfunction

In HIV-negative people, persistent or chronic kidney disease is a risk factor for cardiovascular disease. So researchers at the Veterans Administration (VA) in the United States reviewed their large dataset containing information on more than 17,000 HIV-positive people. Their findings suggest that chronic kidney disease greatly increases the risk for heart attacks in HIV-positive people. What’s more, the tests used to assess kidney health in the VA are relatively simple and routinely used across high-income countries, so the VA findings can be put into use for monitoring kidney health in other countries.

Study details

The VA database contains health-related information on more than 34,000 HIV-positive people. However, the study team focused its analysis on 17,264 people for whom they had extensive data about cardiovascular and kidney health.

The study team used two assessments of kidney health:

- eGFR (estimated glomerular filtration rate)
 - the level of the protein albumin in the urine (albuminuria)
-

For the purposes of this study, the researchers classified eGFR levels as follows:

- normal or mildly reduced kidney function – eGFR of 60 or higher
- moderately reduced kidney function – eGFR between 30 and 59
- severely reduced kidney function – eGFR of 29 or less

The researchers searched their database for events or outcomes such as the following, which occurred between 1999 and 2008:

- hospitalization for heart attack, stroke or peripheral artery disease
- the length of time in the study before a heart attack occurred

In total, there were 1,194 people with reduced kidney function (eGFR less than 60). Their average profile at the start of the study was as follows:

- 2% female, 98% male
- age – 52 years
- high blood pressure – 51%
- diabetes – 15%
- abnormal lipid levels – 25%
- tobacco use – 17%
- albuminuria – 21% had severely elevated levels of albumin in their urine
- hepatitis C virus (HCV) co-infection – 30%
- CD4+ cell count – 267 cells
- 75% were taking anti-HIV drugs

Results—eGFR

The researchers found that, overall, the worse the health of the kidneys, the greater the chance of having serious cardiovascular disease (CVD) issues.

Taking into account many factors—including age, pre-existing CVD risk factors, CD4+ cell count and HIV viral load—having a low eGFR was linked to a significantly elevated relative risk for developing CVD issues as follows:

- eGFR between 45 and 59 – at least a 200% increased relative risk for heart attack or stroke
- eGFR less than 30 – at least a 300% increased relative risk for heart attack or stroke

Looking specifically at eGFR and heart failure, researchers found this link:

- eGFR between 45 and 59 – at least a 200% increased relative risk
- eGFR less than 30 – at least a 300% increased relative risk

For help in understanding relative risk please see the previous story in section B on the DAD study.

Focus on protein in the urine

The study team found the following link between levels of albumin in the urine and a risk for heart attacks:

- albuminuria: 30 mg/dL – a 76% increased relative risk for heart attack
- albuminuria: 100 mg/dL – more than a 300% increased relative risk for heart attack
- albuminuria: greater than 300 mg/dL – more than a 400% increased relative risk for heart attack

The team found that using *both* eGFR and albuminuria strengthened the predictive value of either assessment.

The findings from this VA study are important because they give doctors more tools to help identify HIV-positive patients at high risk for CVD. Furthermore, studies can now be done using eGFR and albuminuria to find ways of reducing the risk for heart attacks in people with chronic kidney disease.

The VA study may also have implications for the timing of the initiation of HAART because other research suggests that HIV can cause kidney damage. Since chronic kidney disease increases the risk for a heart attack, it may be prudent to begin HAART when CD4+ counts are higher than 350 cells. However, the issue of kidney disease and when to start HAART will require a different study.

The VA study is an observational study. Therefore, its findings need to be taken with a degree of caution. However, the link between CVD and chronic kidney disease is well established in HIV-negative people and the finding from the VA linking the same problems in HIV-positive people is not surprising.

A major weakness of this study is the very small proportion of women. The findings from this study, therefore, may not be applicable to HIV-positive women.

Could kidney disease affect DAD's results?

To accompany the publication of the VA results, infectious disease specialist Dr. Paul Sax (Harvard Medical School, Boston) wrote an editorial. He suggests that some doctors may have prescribed abacavir in place of tenofovir for their patients with kidney disease because of the risk of kidney damage from tenofovir. Because chronic kidney disease greatly increases the risk of heart attack, abacavir use in some of these people might have been mistakenly associated with heart attacks. Such a mistaken association might have occurred in DAD, in other studies or in cases where abacavir was prescribed instead of tenofovir because of pre-existing chronic kidney disease.

The findings from the VA are interesting and emphasize the need for monitoring kidney and cardiovascular health and improving the health of these organs in HIV-positive people.

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D. Hepatitis C, HIV and the kidneys

Another team of researchers at the Veterans Administration (VA) in the U.S. conducted an analysis of its dataset, focusing on 23,155 HIV-positive people whose health information had been collected between October 1997 and October 2004. This second VA analysis was interested in finding associations between hepatitis C virus (HCV) infection, HIV and health outcomes such as the presence of kidney disease and survival.

Results

The study team found the following:

- About 40% of HIV-positive people were co-infected with HCV.
- More co-infected participants (14%) had kidney disease compared to people with HIV infection alone (11%).
- After an average of eight years of monitoring, 37% of participants died. Death rates increased as kidney health declined and co-infected people were less likely to survive.

Taking many factors into account, and compared to co-infected people with normal kidney function, having an eGFR less than 60—an indicator of declining kidney health—was highly linked to an increased risk of death, as follows:

- An eGFR between 59 and 30 was associated with nearly a 61% increased risk of death.
- An eGFR between 29 and 15 was linked to a 300% increased risk of death.

The whole picture

The substantially increased risk of death in HIV-HCV co-infected people as kidney health declined is striking. Researchers are not sure why chronic kidney disease amplifies the risk of death. A part of the puzzle is that the study team found that chronic kidney disease could only account for about 25% of deaths in this study. HCV infection could account for a further 25% of deaths. Although not assessed in this study, the team suspects that other factors, such as substance use and complications from a failing liver (due to HCV infection), may have been partly responsible for the unusually high death rate in this study.

The VA analysis should stimulate initiatives to improve medical care for co-infected people, specifically ensuring that they receive HAART as well as therapy for HCV infection and complications such as depression, heart and kidney disease.

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E. Tenofovir and the kidneys

The anti-HIV drug tenofovir (Viread, and in Atripla and Truvada) is an effective part of combination therapy for HIV.

The kidneys process tenofovir and there have been rare cases of tenofovir users developing serious kidney dysfunction. To investigate this problem, researchers from the U.S. health care organization Kaiser Permanente reviewed their large database of information on HIV-positive people who initiated anti-HIV therapy with or without tenofovir. They found that some tenofovir users had a detectable and significant decline in kidney health. These and other details appear in this report.

Study details

Researchers reviewed data from databases in California, Maryland, Virginia and Washington, DC. All participants began taking HAART between January 2002 and January 2006. In total, the researchers focused their analysis on data from 964 HIV-positive people who were taking tenofovir and 683 people who were not.

Tenofovir can damage part of the kidney called the renal tubules. The damage causes proximal renal dysfunction, which can lead to reduced efficiency filtering the blood, the loss of key nutrients and other problems such as the following:

- detectable protein in the urine (proteinuria)
- sugar in the urine (glucosuria)
- less-than-normal levels of the mineral phosphorus in the blood (hypophosphatemia)
- phosphorus in the urine (phosphaturia)
- acidic blood (serum acidosis)
- less-than-normal levels of potassium in the blood

Researchers checked eGFR (estimated glomerular filtration rate) to get an idea of how the kidneys were working. They divided people into the following two groups:

- tenofovir-exposed group – 964 people
- tenofovir-sparing group – 683 people

Apart from their use (or not) of tenofovir, the two groups of people were broadly similar, with the following average profile:

- 14% female, 86% male
- age – 30 years
- CD4+ count – 205 cells

- HIV viral load – 63,000 copies
- eGFR – 100

Results

A high proportion of people in both groups achieved a suppressed viral load as follows:

At one year:

- tenofovir-exposed group – 94%
- tenofovir-sparing group – 97%

At two years:

- tenofovir-exposed group – 93%
- tenofovir-sparing group – 96%

These differences between groups were statistically significant. However, it is important to bear in mind that several randomized clinical trials have found that tenofovir-containing regimens have potent anti-HIV activity. So this particular finding from the Kaiser analysis is puzzling and unexpected and should be read with caution.

Kidney function

Creatinine is a waste product that is removed from the blood by the kidneys. When these organs are malfunctioning, creatinine levels in the blood can rise. Modest increases in blood levels of creatinine were more likely to occur in tenofovir users. But it is important to note that large increases in creatinine were not confined to tenofovir users. Indeed, people who had large increases in creatinine tended to have the following features:

- older age
- low CD4+ counts (less than 50 cells)

Significantly more people using tenofovir developed proximal tubular dysfunction (8%) compared to people not taking tenofovir (4%). Furthermore, there was an increase in this problem over time, with the risk of proximal tubular dysfunction increasing among tenofovir users as follows:

- week 26 – 19% increased relative risk; not statistically significant
 - week 44 – 61% increased relative risk; not statistically significant
 - week 52 – 95% increased relative risk; statistically significant
 - week 104 – 500% increased relative risk; statistically significant
-

Among people who developed proximal tubular dysfunction, 21% stopped taking tenofovir.

Putting it in perspective

The findings from this Kaiser study are interesting but several points need to be taken into account when considering the results, including these:

- This was a cohort study, which is good at finding associations. But this study cannot prove that tenofovir caused any of the kidney problems detected. This is because in analyzing such studies, the problem of confounding or channeling bias can arise, making it difficult to draw firm conclusions.
- The associations found in a cohort or observational study can be later explored in a clinical trial of a more robust design, such as a randomized trial. However, bear in mind that data from clinical trials suggest that, for most people, tenofovir is a safe and effective part of combination therapy.

It is not clear why in the present Kaiser analysis tenofovir was associated with more problems than reported in other trials. It might be that the Kaiser team was unable to account for potential confounding data such as the use of other drugs, which could increase the risk of kidney damage. Such drugs can include the following prescription and non-prescription medications:

- several antibiotics
- several antiviral drugs
- several antifungal drugs
- pain medicines, including acetaminophen (Tylenol) and ibuprofen (Advil, Motrin)

For a more detailed list of drugs with the potential to cause kidney toxicity, please see CATIE's in-depth Fact Sheet on tenofovir available at:

www.catie.ca/facts.nsf/9a83231f2055bda9852566b90004b064/a5552a3146cf5c8185256c2f005a588a!OpenDocument

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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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What CATIE Does

CATIE (the Canadian AIDS Treatment Information Exchange) is committed to improving the health and quality of life of all people living with HIV/AIDS in Canada. CATIE serves people living with HIV/AIDS, and the people and organizations that support them, by providing accessible, accurate, unbiased and timely treatment information. CATIE provides such information through a comprehensive Web site, a bilingual toll-free phone service, electronic and print publications, a national reference library and workshops and exhibits at conferences across Canada.

CATIE Publications

TreatmentUpdate

CATIE's flagship treatment digest on cutting-edge developments in HIV/AIDS research and treatment. Subscribe to TreatmentUpdate and automatically receive an email notifying you the moment a new issue is available on-line or contact us at 1.800.263.1638 to receive a print subscription.

A Practical Guide to HAART

The latest on what is known about the various aspects of treatment, including a description of the virus and the immune system, the stages of HIV disease, the tests used to assess health status, and anti-HIV medications.

A Practical Guide to HIV Drug Side Effects

The latest on what is known about various side effects related to treatment, from appetite loss to sexual difficulties, and tips for countering or preventing them.

The Practical Guide series also includes:

- A Practical Guide to Nutrition
- A Practical Guide to Complementary Therapies
- A Practical Guide to Herbal Therapies

The Positive Side magazine

Holistic health information and views for PHAs.

Fact Sheets & Supplement Sheets

Concise overviews of conditions, symptoms, medications, side effects, complementary therapies, vitamins, herbs and other treatment issues.

pre*fix

A harm reduction booklet for HIV+ drug users.

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