I HIV PREVENTION

A. Getting to know PEP and PrEP

In Canada and other high-income countries, the widespread availability of potent combination therapy for HIV, commonly called ART or HAART, has made deaths due to AIDS-related infections uncommon compared to the time before such therapies were available. Moreover, the benefit of ART is so profound that researchers expect that someone who is infected and diagnosed today and does not have other serious health conditions will likely live a near-normal life span.

ART, combined with a range of other measures, can significantly reduce the risk of HIV transmission from an HIV-positive mother to her baby. Anti-HIV drugs are taken by the mother-to-be during pregnancy and birth and then given to the baby for several weeks after birth.

In a clinical trial called iPrEx, a combination of anti-HIV drugs—tenofovir and FTC—sold in a fixed-dose pill called Truvada was found to reduce the risk of becoming HIV positive by 44% among gay and bisexual men and transgender women, compared to placebo. Some other clinical trials have found PrEP to reduce the risk of HIV infection for heterosexual men and women.

These examples show that anti-HIV drugs can help reduce the risk of infection. Taking anti-HIV drugs before being exposed to the virus is called pre-exposure prophylaxis (PrEP). Taking anti-HIV drugs after possible exposure to HIV to prevent infection (as is the case with babies born to HIV-positive mothers or in people who may have been exposed to HIV through needle-stick injuries or sexual exposure) is called post-exposure prophylaxis (PEP).
In this issue of *Treatment Update*, we feature several reports on PrEP from high-income countries such as Canada, Australia, the Netherlands and the United States.

### B. Asking about sexual behaviour and PrEP in Toronto

At press time, Health Canada has not approved the use of any anti-HIV drug for the purposes of PrEP. Currently, the American Food and Drug Administration (FDA) is considering the approval of Truvada as PrEP. Some public health departments in California are conducting observational studies of PrEP among men who have sex with men (MSM), and in France a trial of intermittent PrEP among MSM is underway. It is possible that such observational or other types of PrEP studies could come to Canada or that Truvada as PrEP may be approved by Health Canada one day. Before PrEP becomes licensed, it is important to find out what sexually active gay and bisexual men know about it and whether they are currently using it. This latter possibility is occurring in some American cities, according to anecdotal reports.

Leading infectious disease researcher Darrell Tan led a team that surveyed sexually active men undergoing HIV testing at a sexual health clinic in downtown Toronto about their sexual behaviour and PrEP. Of the 256 men surveyed, nearly 12% knew about PrEP, particularly men who have sex with men. None of the men disclosed any use of PrEP and many were interested in the future use of PrEP, should it be licensed in Canada.

#### Study details

The study was done in cooperation with the staff at Toronto's Hassle Free Clinic. Participants were all undergoing rapid HIV testing and they all had negative results.

In total, 256 men completed the survey. Participants were either men who had sex with men (MSM) or men who had sex with women (MSW). About 90% of the men were between the ages of 20 and 50 years.

#### Results—Sexual behaviours

More MSM (39%) had five or more sexual partners within the past six months compared to MSW (20%).

Of all the common sexual behaviours, unprotected anal sex carries the greatest risk for HIV transmission, so the research team enquired about this.

- When asked if they had unprotected anal sex in the past six months, 53% of MSM disclosed that they did. Among MSW, the figure was 21%.
- Roughly 27% of MSM and 12% of MSW disclosed that in the past six months they engaged in unprotected anal intercourse while under the influence of alcohol.
- About 10% of MSM and 5% of MSW disclosed that in the past six months they had unprotected anal intercourse under the influence of both alcohol and drugs.

#### Questioned about PrEP

About 14% of MSM and 5% of MSW reported that they had heard of PrEP. This difference was statistically significant.

When the men were asked if they would be willing to use PrEP if it was “proven safe and effective,” many men, particularly MSM, were willing to do so. None of the men in the study had used PrEP.

A similar recent study in New York City that recruited 554 MSM from two of the city’s bathhouses found that 60% of MSM had unprotected anal sex in the past three months. About 36% of participants were aware of PEP or PrEP. Both the Toronto and New York City studies show that there is an urgent need to intensify HIV prevention activities.

The Toronto researchers stated: “Determining whether, where, when and how to optimally roll out PrEP will require a multi-stakeholder process to ensure [that] optimal strategies for financing, administering and monitoring this promising new HIV prevention strategy are developed.”

#### Important facts about using PrEP

The results of the iPrEx study show that when used for about one year, Truvada can provide partial protection against HIV infection, at least among high-risk MSM. However, before embarking on widespread use of Truvada as PrEP, there are several issues to consider.

1. **Condoms are still needed**

   Truvada is only modestly effective in preventing HIV infection and cannot replace safer sex.

   Dr. Kevin Fenton, director of the National Center for HIV/AIDS at the American Centers for Disease
Control and Prevention (CDC), says that the iPrEx data are “encouraging,” however, he adds, “this is not the time for gay men to throw away their condoms.”

2. Resistance and reduced treatment options
People using PrEP require frequent HIV testing. It is very important that people considering PrEP are not infected with HIV because of the risk of developing drug resistance. More than 25% of people living with HIV in Canada are not aware of their HIV status. Furthermore, the risk of resistance may be greatest during acute HIV infection, when conventional HIV tests cannot detect infection.

3. Hepatitis B virus
Hepatitis B virus (HBV) can be sexually transmitted, particularly among MSM. Men who are interested in using PrEP need to first be screened for HBV infection; if found negative and unvaccinated, they should be given the vaccine to protect them from this virus. Truvada also possesses anti-HBV activity. As a result, it can help place chronic HBV infection into remission. Among people with chronic HBV, suddenly stopping treatment, such as Truvada, can cause HBV to come out of remission and affect a person’s health.

4. Effectiveness of PrEP in other populations
The iPrEx study involved MSM who were at high risk for HIV infection. The primary mode of exposure to HIV was through rectal tissue during unprotected receptive anal intercourse. According to the investigators, this study does not provide any information about effectiveness or safety of PrEP for vaginal, penile or intravenous exposure to HIV. Further studies are needed to determine if PrEP has any effect in reducing HIV transmission from heterosexual vaginal sex, intravenous drug use or insertive anal sex.

5. Safety and use in the real world
We don’t know how willing gay and bisexual men will be to take PrEP over the long term. We know from people living with HIV that taking anti-HIV drugs on a regular basis is a challenge and can lead to long-term side effects that are difficult to manage. Truvada can affect the health of the kidneys and bones in HIV-positive people. Commonly used over-the-counter drugs such as acetaminophen (Tylenol) and ibuprofen (Advil, Motrin) can also affect kidney health.

PrEP must be provided within the context of a comprehensive prevention program. The iPrEx trial participants were frequently monitored for sexually transmitted infections (STIs), HIV and drug toxicity. They were also offered regular HIV risk counseling and adherence support. In the “real” world outside the clinical trial, for PrEP to work, people on PrEP will need close medical supervision, regular safer-sex counselling, and frequent testing for HIV and STIs. Some HIV-negative men may feel that this level of bio-medical intervention is too intrusive.

6. PrEP and risk behaviour
Another concern is that some people may feel a false sense of security when using PrEP and may decide to engage in more risky activities. If people using PrEP have sex with more partners, use condoms less often, or share needles more frequently, their overall risk for HIV infection (and other STIs) may increase because PrEP does not provide complete protection.

7. Cost
Currently, PrEP is a very expensive intervention. A one-month supply of 30 Truvada pills costs at least $800 in Canada or the U.S.—$27 per day.

8. Unsupervised use of PrEP
PrEP involves taking anti-HIV drugs. These medications must be prescribed and monitored by a doctor, who can provide them in a safe and informed way. Some people may be tempted to experiment with drugs obtained from other sources—from a friend, people at parties, or over the Internet. This could be harmful. Incorrect use of anti-HIV drugs can cause HIV drug resistance. It might also cause serious, even life-threatening, reactions in some people. Anti-HIV drugs can interact with prescription drugs, recreational drugs and other substances. These interactions can be harmful, even when there are no symptoms.

PrEP resources

CDC Statement on Results of iPrEx Trial: www.cdc.gov/nchhstp/newsroom/iPrExMediaStatement.html

CATIE Fact Sheet on Truvada is available at: http://www.catie.ca/en/fact-sheets/co-formulations/truvada
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C. Unexpected effects of PEP in Amsterdam

SIV (simian immunodeficiency virus) is related to HIV, and in susceptible monkeys SIV causes an AIDS-like condition. Experiments with monkeys have found that giving them anti-SIV drugs shortly after they are exposed to SIV greatly reduces their risk of becoming infected with that virus. This use of medicines shortly after exposure to a germ to prevent infection is called post-exposure prophylaxis (PEP).

Animal studies also suggest that PEP is most effective the sooner it is used after exposure, within a maximum of 72 hours post-exposure. PEP must be taken every day for four consecutive weeks to prevent HIV infection.

In most high-income countries, including Canada, PEP is freely available after a work-related exposure such as a needle-stick injury among health care workers. However, the use of PEP is not generally subsidized for accidental exposure because of consensual sex in Canada. Still, PEP combined with intensive counselling about risk behaviour may be a useful way of helping to limit the spread of HIV among sexually active people who are at high risk for HIV infection, particularly men who have sex with men (MSM).

Researchers in Amsterdam have been studying two groups of men, as follows:
- MSM who have received PEP because of possible exposure to HIV arising from consensual sex
- MSM who did not receive PEP but were being monitored to assess changes in their HIV infection status over time

Over the past decade, the Dutch researchers found that the rate of HIV infection among MSM generally increased. However, the rate of HIV infection among PEP users was significantly greater. This latter finding, together with disclosure of behaviours by participants, suggests that PEP users in Amsterdam continued to engage in unprotected anal intercourse after their course of PEP was complete. The results of the Dutch study demonstrate the need for more intensive counselling for MSM who use PEP to help protect them from HIV infection.

Study details
Men who sought PEP were first tested for HIV and, if negative, were prescribed a 28-day course of anti-HIV medicines. These men were also retested for HIV three and six months after their first HIV test within the study.

Whenever possible, doctors prescribed simple and tolerable combinations of drugs for PEP. As the study lasted for about a decade, the medicines used in PEP changed over the course of time as new drugs were approved for use.

Simultaneously with the PEP study, the research team was also conducting the Amsterdam Cohort Study (ACS). As part of the ACS, MSM not part of the PEP study were enrolled; they were monitored and regularly tested for HIV. The ACS took place over the same period as the PEP study. The findings of the ACS were used as a point of reference for estimating risks of HIV infection and assessing risk behaviours in other studies, such as the PEP study.

Results—PEP prescriptions
During the decade-long Dutch study there were 395 prescriptions for PEP that arose from possible sexual exposure to HIV among MSM in Amsterdam. A total of 355 men received one prescription for a 28-day course of PEP. The remaining MSM received between two and four prescriptions for PEP.
Prescriptions for PEP were distributed as follows:

- 61% of cases were exposed via unprotected receptive anal intercourse
- 37% of cases disclosed that exposure occurred with a sex partner known to be HIV positive

Most PEP users (86%) reported side effects. However, researchers stated that “the vast majority [94%] completed their PEP course.”

**HIV infections**

The Dutch PEP study was observational in nature and was not designed to, nor can it, assess the effectiveness of PEP. However, it seems that PEP was generally effective. A total of 11 men became HIV positive during the PEP study. These men were initially HIV negative but became HIV positive between three and six months after having used PEP. Moreover, most of these men disclosed that they had engaged in high-risk sexual behaviour after completing their course of PEP. Also, assessment of HIV among the 11 men who become HIV positive found that their virus was not resistant to treatment, which would have been likely had PEP failed to protect them.

Among 782 participants in ACS, the risk of HIV infection was about four times less.

When researchers examined specific periods of time over the course of their studies, they found that rates of new infections were similar in both groups of MSM around the year 2000 but by 2009, rates of infection had significantly diverged, increasing among the men given PEP.

Studies in Australia among MSM have found broadly similar trends, with more cases of HIV occurring in the recent era, particularly among PEP users.

The Dutch researchers found that some MSM requesting PEP presumed that they were HIV negative but rapid testing revealed that they were in fact HIV positive. This finding suggests that they had been infected prior to their most recent episode of unprotected sex. This underscores the need for sexually active adults to get frequent HIV tests if they are having unprotected intercourse.

The trend of increasing HIV infections in both the ACS and the PEP study indicates that high-risk behaviours are continuing in the present era when ART is widely available and that simply prescribing PEP to people is not sufficient to halt the spread of HIV over the long term.

**What is to be done?**

The Dutch researchers call for “a combination of more comprehensive preventive strategies,” including counselling, for MSM who engage in unprotected intercourse. In another study where men who were exposed to HIV were given counselling and PEP, 77% of participants reported a decline in unprotected sex after counselling.

The men in the present study who engaged in unprotected intercourse may also be good candidates for pre-exposure prophylaxis (PrEP) should this intervention become available.

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**II HEPATITIS**

**A. Hepatitis E virus**

Infection with hepatitis E virus (HEV) is uncommon but apparently emerging in the high-income regions of North America, Western Europe and Australia. However, HEV is relatively common in parts of Asia, Africa and Central America. In these regions, HEV is commonly spread to people when sewage contaminates drinking water supplies. HEV can be associated with symptom-free infection or more severe symptoms associated with viral hepatitis, such as the following:

- fever
- chills
- yellowing of the skin and whites of the eyes
• dark urine
• loss of appetite
• nausea
• vomiting
• abdominal pain
• muscle, bone and joint pain
• headache

In high-income countries, cases of HEV have been linked to eating undercooked products made from certain animals such as these:

• pigs (including pig liver and sausages)
• wild boar
• deer

(Ken Sherman, MD, University of Cincinnati College of Medicine, personal communication)

Another source of exposure to HEV is recent travel to a region where HEV infection is relatively common.

Most cases of HEV resolve without intervention. In rare cases treatment has been necessary and there are reports of successful recovery when the broad-spectrum antiviral agent ribavirin has been used, with or without interferon-alpha.

In most cases of HEV infection in people in high-income countries, this virus does not appear to cause chronic disease that leads to liver damage. However, in the past decade, research teams in Western Europe have been reporting clusters of HEV infection in people with weakened immune systems due to cancer and organ transplantation. In these particular cases, liver damage has occurred.

Due to these reports, other research teams have been concerned that people whose immune systems are weakened from HIV infection may also be at risk for becoming infected with HEV and developing liver damage. Here are findings from several studies by those other research teams.

United Kingdom
A team in the southern UK at hospitals in Truro and Bristol tested blood samples from 138 HIV-positive people and 463 HIV-negative people for antibodies to HEV—suggesting exposure to this virus. They were also tested for HEV’s genetic material using PCR (polymerase chain reaction); this is suggestive of active HEV infection. The team found no differences in rates of exposure to HEV between the two populations studied. Moreover, no HIV-positive people had chronic HEV infection.

France
A large team of researchers in both northern and southern France—in towns and cities such as Hyères, Maison-Alfort, Marseille, Pau, Paris and Toulon—conducted a study with 245 HIV-positive people. Using antibody and PCR testing, technicians found that about 3% of people from northern France had been exposed to HEV in the past, compared to about 9% in southern France. No cases of chronic HEV infection were found among HIV-positive people.

Switzerland
Researchers in this country tested 735 HIV-positive people who had unexplained elevations in ALT for exposure to HEV. They found that about 3% of people had been exposed to this virus. None of the people in this study had infection with hepatitis B or C viruses. Only one patient had chronic HEV infection, lasting for 24 months while he had a low CD4+ count (less than 100 cells). Once he began ART and his CD4+ count rose, he recovered from HEV infection.

United States
One study to investigate HEV infection among HIV-positive people was done by a consortium of military medical researchers in the U.S. Researchers analysed stored blood samples that had been collected between 1985 and 2009 because people had been having elevated levels of the liver enzyme ALT (alanine aminotransferease) in the blood by at least five times above the upper limit of normal. Elevations of such magnitude are suggestive of liver injury, such as that caused by viral infection of the liver. The research team scoured the medical records of 4,410 HIV-positive people and found blood samples from 194 that were available for HEV testing. In total, testing revealed that 13 people had been exposed to HEV.

There were no increases in HEV infections between 1985 and 2009. In general, there were no differences in the characteristics of people exposed to HEV and those who were not. The exception was that HEV-positive people tended to have higher HIV viral loads than HEV-negative people. None of the 13 HEV-positive people developed chronic HEV infection.

Taken together, the results from these studies suggest that HEV does not seem to be more common among HIV-positive people.
Suspecting HEV

Several of the research teams mentioned above, including the American one, have proposed that a diagnosis of HEV infection be considered for people with symptoms or lab tests suggestive of “viral-like hepatitis.” Antibody testing for HEV may return with a negative result despite ongoing HEV infection. Therefore, the U.S. team suggests that among HIV-positive people, particularly those with low CD4+ cell counts, PCR testing should be used to assess HEV infection status. Furthermore, they add that HIV-positive people who take ART may be better able to recover from HEV, but this needs to be proven in a study.

Further general research on HEV is being done by the U.S. Centers for Disease Control and Prevention (CDC) as well as by scientists in Western Europe.

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B. Managing side effects from new hepatitis C drugs

Boceprevir (Victrelis) and telaprevir (Incivek) are newly licensed treatments for hepatitis C virus (HCV) mono-infection (HCV infection only). Clinical trials are planned or underway testing these drugs in people who are co-infected with HCV and HIV. These drugs are meant to be used in combination with interferon-alpha and ribavirin.

The goal of anti-HCV therapy is to maximize the chances of curing HCV infection. Bearing this in mind, physicians are likely to continue therapy in the face of drug side effects provided that they are not life-threatening.

As with all new drugs, the full range of side effects and drug interactions may not be known for several years. Based on an analysis of Phase III trials of boceprevir and telaprevir, French liver specialist Dr. Christophe Hézode (Université Paris Est) has provided guidance for physicians caring for people who develop side effects while taking these new drugs. We encourage readers to note that while side effects with anti-HCV therapy are common, those caused by boceprevir and telaprevir are generally manageable.

Telaprevir

Common side effects with this drug include the following:
- rash
- itchy rash
- anemia
- gastro-intestinal symptoms – nausea, diarrhea and anal itching
Boceprevir
Common side effects with this drug include the following:

• fatigue
• anemia
• nausea
• diarrhea
• change in sense of taste
• lower-than-normal levels of neutrophils (a type of white blood cell) in the blood

Anemia
Red blood cells (RBCs) help to carry oxygen to tissues and remove the waste product carbon dioxide. When RBC levels fall below normal, people can become tired easily. In more severe cases, fatigue, shortness of breath, dizziness and headache can develop. Anemia can occur because the anti-HCV drug ribavirin can cause these cells to prematurely die. In clinical trials, about 20% of people who received boceprevir or telaprevir developed anemia.

RBCs carry an iron-containing protein called hemoglobin, which gives blood cells (and blood) its characteristic deep red colour. To assess anemia, hemoglobin levels in blood samples are measured—levels less than 10 g/dl indicate anemia.

Anemia did not apparently have an effect on recovery from HCV among telaprevir users. However, among participants who received boceprevir, recovery from HCV was more likely if participants developed anemia. The reason for this link between recovery and anemia on boceprevir is unclear.

Depending on the severity of anemia that occurs, doctors have several options:

• closely monitor affected patients to see if anemia is limited or becomes worse
• prescribe the injectable hormone EPO (erythropoietin) – it can stimulate the bone marrow to produce more RBCs
• lower the dose of ribavirin once HCV viral load has been suppressed – results from clinical trials exploring either reducing the dose of ribavirin (once HCV viral load has been suppressed) or providing injections of EPO should be available later in 2012

HCV and the skin—Problems appear before treatment
In the past two decades researchers have become aware that HCV infection can be associated with skin problems. A large French study with 1,614 participants (56% men, 46% women) found that the following skin problems occurred even before patients received treatment:

• psoriasis – 3%
• itchy skin – 15%

The reasons for this are not clear but this link with HCV infection and skin problems is important to bear in mind.

Skin problems with interferon and ribavirin
Before the approval of specific anti-HCV drugs such as boceprevir and telaprevir, standard therapy for HCV consisted of a combination of interferon-alpha and ribavirin. These two drugs can also cause skin problems, such as generalized itchy rash or dry skin or sometimes a combination of both. In some cases, the affected skin may develop temporary red lesions. In most cases, these can be managed with prescription anti-inflammatory creams containing corticosteroids. As the rash subsides, patients can switch to using moisturizers.

Skin problems and telaprevir
Data from clinical trials suggests that telaprevir can affect the skin—causing rash and other skin-related problems in about 50% of participants. The vast majority of rashes were of mild-to-moderate intensity, involving less than 30% of the skin. Generally such rashes did not become worse. The rash seen with telaprevir was generally similar to rash seen with interferon and ribavirin, however, telaprevir-associated rash tended to be more frequent and more severe.

Rash related to telaprevir can occur at any time while the drug is being used. Researchers have found that 50% of telaprevir-related rash occurred during the first four weeks of use. Even if therapy is stopped, it may take several weeks before rashes completely resolve.
Dr. Hézode has suggested the following staging system for mild-to-moderate rash associated with telaprevir:

- **mild rash** – close medical monitoring to see if it gets worse
- **moderate rash** (affecting less than 50% of the skin) – consider referring the patient to a dermatologist
- **worsening rash** – the physician should consider permanently discontinuing telaprevir. If rash does not resolve within a week of discontinuing telaprevir, then interrupt ribavirin therapy while continuing interferon-alpha.

According to Europe-based HCV researchers, in cases of mild-to-moderate rash, corticosteroid-containing creams and certain antihistamines, including the following, may be used:

- diphenhydramine (Benadryl)
- hydroxyzine (Atarax)
- levocetirizine (Xyzal)
- desloratadine (Clarinex)

### How to use moisturizer

Moisturizing creams rather than lotions or ointments “may be effective in relieving [very red, itchy and swollen skin],” says Dr. Hézode. He and other leading HCV researchers recommend the following regimen: “Cream should be applied for at least 15 minutes, beginning with areas around the hands, feet and the skin around the large joints”… “And progressing with broad strokes across the rest of the skin. This should begin 15 minutes after showering or bathing and should be applied daily.” Other rash-relieving tips: Limit exposure to sun and heat. Take baking soda or oatmeal baths. Wear loose-fitting clothes.

### Serious rashes

Severe rashes appeared to be more common among users of telaprevir than among people who used interferon and ribavirin. In about 5% of clinical trial participants, telaprevir-associated rash was severe. As with every drug, there are always cases of very severe skin reactions that could become life threatening if early symptoms go unrecognized and if use of the drug is not stopped.

The good news is that in the case of telaprevir only about 0.4% of participants developed a collection of severe rash and other symptoms called DRESS (drug reactions with eosinophilia and systemic symptoms) and TEN (toxic epidermal necrolysis) or Stevens-Johnson Syndrome (SJS). All severe reactions cleared once participants stopped taking telaprevir.

### About DRESS

In general, cases of DRESS tend to occur several weeks after a person has started taking the offending drug. DRESS involves an immunologic reaction that can affect several parts of the body (liver, kidneys, lungs, heart), depending on the severity of the reaction.

There does not appear to be international consensus about all the signs and symptoms associated with DRESS. However, cases of DRESS have been associated with the following:

- fever (more than 38.5°C)
- rash
- swollen lymph nodes
- facial swelling
- higher-than-normal levels of liver enzymes in the blood
- eosinophilia – an increase in the number of a type of white blood cell called eosinophils in blood and tissues

Due to the similarities between some symptoms of DRESS and infections, a delay in arriving at an accurate diagnosis sometimes occurs.

DRESS can cause severe complications when it affects internal organs (liver, kidneys, lungs, heart).

### About SJS and TEN

SJS and TEN have similar symptoms. Prior to SJS occurring, patients may experience a flu-like illness with such symptoms as these:

- cough
- fever
- sore throat

A few days later the following can occur:

- swelling of the face and/or tongue
- painful skin
- raised itchy and red patches of skin
- a rapidly spreading red or purple skin rash
- blisters on the skin, particularly in the mouth, inside the nose and eyes
- the outer layers of the skin start to fall off
SJS and TEN can cause life-threatening complications, so if symptoms occur, contact your physician right away or go to the emergency department of a hospital.

**Anal problems**

In placebo-controlled studies, anorectal problems were more common among telaprevir users (26%) than among people who received placebo (5%). Anorectal problems included the following:

- hemorrhoids
- anal itching
- anal discomfort
- rectal burning

Mostly these problems were of mild-to-moderate intensity and they cleared after the course of telaprevir treatment ceased.

Dr. Hézode recommends that patients who use telaprevir and who report these problems first have their physicians conduct an anal exam to assess the health of the affected area and rule out other possible causes of anal irritation. He recommends anal creams, corticosteroid creams and even local anaesthetic creams in cases of rectal burning.

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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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Writer Sean Hosein
Editor RonniLyn Pustil

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Contact CATIE
by e-mail: info@catie.ca
on the Web: www.catie.ca
by telephone: 416.203.7122
1.800.263.1638 (toll-free)
by fax: 416.203.8284
by post: 505-555 Richmond Street W
Toronto, Ontario
M5V 3B1
Canada

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