

Heart disease and antiretroviral therapy

by Dr. Marek Smieja and Linda Robinson

We know that antiretroviral (ARV) therapy is life saving and improves quality of life, but there have been concerns that some ARVs increase the long-term risk of heart attack. To help answer that question, the DAD Cohort Study has monitored 33,000 HIV-positive people for heart attacks since 1999.

The DAD Study found that heart attacks increase over the years while a person is on ARV treatment, especially with protease inhibitors (PIs). We know that many of these drugs affect blood cholesterol and blood glucose, which could affect heart risk. Last year, the DAD Study produced findings suggesting that abacavir (Ziagen®, also in Kivexa®) and didanosine (Videx®) — which are nucleoside reverse transcriptase inhibitors (NRTIs) — also increased heart attacks. In randomized trials, abacavir hasn't shown any increased heart attack risk, but the number of cardiac events in these trials was too low to measure the risk precisely.

In an observational study like DAD, drug regimens are freely chosen by doctor and patient. There's always a chance that patient characteristics influence the selection of medication and also influence outcomes.



New data from CROI 2009

This year, at the Conference on Retroviruses and Opportunistic Infections (CROI) in Montreal, the DAD Study investigators presented new data on individual drugs and the risk of heart attack. For PIs, indinavir (Crixivan®) and lopinavir/ritonavir (Kaletra®) increased heart attack risk, while saquinavir (Invirase®) and nelfinavir (Viracept®) did not. The addition of ritonavir didn't seem to affect risk. Not enough information was available on atazanavir (Reyataz®), amprenavir (Agenerase®) or darunavir (Prezista®) to report their risk profiles.

No excess risk was observed for the non-nucleoside reverse transcriptase inhibitors (NNRTIs), efavirenz (Sustiva®) and nevirapine (Viramune®). For NRTIs, excess risk was seen for abacavir (Ziagen®) and didanosine (Videx®), but not for tenofovir (Viread®), lamivudine (3TC®), stavudine (Zerit®) or zidovudine (Retrovir®).

Dr. Marek Smieja is an infectious disease physician and HIV consultant at McMaster University in Hamilton.

Linda Robinson is a pharmacist at the Windsor Regional Hospital.

Should you change treatments?

For most people, the baseline risk of a heart attack (meaning the risk before taking ARV treatment into account) is very small (on average, 0.3 percent per year); even if an ARV doubled that risk, it may not be a major concern. If you're at low risk for heart attack, you and your doctor may decide to continue a therapy that's working well.

However, if you're at high risk for heart disease, switching drug therapy or starting on a statin drug (to lower cholesterol) along with your current therapy may minimize your long-term risk. These options should be discussed with your doctor and pharmacist. But never stop antiretroviral therapy in hopes of avoiding a heart attack: the SMART (Strategies for Management of Antiretroviral Therapy) study showed that stopping treatment increases heart attacks!

Control other risk factors

Risk factors for heart disease can be divided into the uncontrollable (age, sex, family history) and controllable (smoking, cholesterol, blood pressure, and healthy lifestyle). Men over 45 and women over 55 are at greater risk. Make sure your doctor is monitoring for changes that may be related to ARVs, and seek help to make heart-healthy lifestyle choices: quit smoking, eat well, and exercise.

Quit smoking, eat well, get moving

Smoking cigarettes triples your risk of heart attack — far more than the effect of any ARV — and even second-hand smoke is dangerous. Fortunately, if you want to quit, there are many effective smoking cessation programs, tools and medications to help. If you relapse, keep trying: most successful quitters tried more than once. If you're a heavy smoker, even cutting down might help to prevent a heart attack.

Cholesterol (lipids) and blood sugar can be affected by diet. Request an appointment with a dietician who's familiar with HIV to help you plan meals, and increase your consumption of fruits, vegetables, fibre and fish.

Regular exercise, even if it's as simple as walking for 30 minutes a day, lowers lipids, blood sugar and blood pressure, and helps maintain a healthy weight.

Don't miss your appointments

Regular medical exams and lab tests not only help monitor your HIV treatment, but also your lipids, blood sugar and blood pressure, all of which are controllable risk factors for heart disease. **R**

The ABCs of viral hepatitis

How to prevent and treat liver infections when you have HIV

by Dr. Marina B. Klein



The question “Have you ever had hepatitis?” isn’t always easy to answer. There are several different types, each with its own letter; they’re transmitted in different ways; some are curable while others aren’t. But the details are important. If you’ve had hepatitis in the past, this could influence the choice of treatment for HIV. If you haven’t, there are practices and, sometimes, vaccines that can prevent you from becoming infected. This article looks at the three most common types of viral hepatitis, all of which can be detected and evaluated using simple blood tests.

Hepatitis A

Hepatitis A is a common form of viral hepatitis, found in North American and tropical countries. It’s transmitted by exposure to fecal material, either by eating food prepared by someone who didn’t wash their hands after using the bathroom or drinking contaminated water. It’s highly infectious and most commonly acquired when travelling to countries that have high rates of infection. It can also be passed on through sexual intercourse, particularly oral sex or anal sex with a person who’s in the active phase of infection. Between 15% and 60% of Canadian adults over age 30 have been exposed to hepatitis A. Aboriginals, immigrants and men who have sex with men (MSM) have higher rates.

Severe but passing symptoms

Hepatitis A tends to be the least harmful of the three. Most people who become infected will have

symptoms of severe fatigue, nausea, vomiting, pain and swelling of the liver, jaundice (yellowing of the skin and eyes) and dark urine. Although these symptoms can be quite severe, they almost always resolve on their own and rarely result in severe damage to the liver. Once the symptoms are gone, the infection is considered cured and a person is protected from getting infected again. There's no chronic form of hepatitis A.

Hepatitis A can be particularly severe and occasionally life-threatening for people who also have another form of chronic hepatitis (e.g. hepatitis B or C).

Hepatitis A infection is diagnosed by testing for antibodies in your blood. During acute infection, concentrations (titres) of IgM antibodies are high. When the infection resolves, IgG antibodies appear and persist life-long. These indicate that you're now protected from being infected with hepatitis A again, but they don't protect you from hepatitis B or C. (See sidebar on page 12 for more on testing).

Prevention

Hepatitis A infection can be prevented with a vaccine (Havrix™, or in combination with hepatitis B vaccine in the form of Twinrix™). All persons with HIV who've never had hepatitis A (e.g. in whom IgG antibodies are negative) should receive the hepatitis A vaccine, particularly MSM and those with other chronic hepatitis infections.

Hepatitis B virus (HBV)

Hepatitis B infection, although less common than hepatitis A, can be much more serious. Hepatitis B infection has both acute and chronic phases, and about 5% to 8% of Canadians infected with HIV are also chronically infected with HBV.

HBV is mainly transmitted in much the same way as HIV — from mother to child, by sexual contact or percutaneous (under the skin) blood exposure (e.g. injection drug use or tattoos). HBV is the most contagious of any of the hepatitis viruses (about 100 times more infective than HIV), so household members and sexual partners of persons chronically infected with HBV are at high risk for acquiring this infection unless they've been vaccinated.

Worse if you have HIV

Acute infection with HBV produces symptoms similar to hepatitis A, but these can be far more severe and in some cases life-threatening. In most people, the infection will resolve, but in others it doesn't and the infection becomes chronic. People living with HIV who acquire HBV will develop chronic

infection about 25% of the time — a much higher rate than people who don't have HIV. Chronic infection will persist lifelong and, if untreated, can lead to serious liver damage including cirrhosis (scarring of the liver), liver failure and liver cancer. It can also be passed on to other people. Like hepatitis A, HBV can be diagnosed with blood tests, which can also determine if the infection is acute or chronic and measure the level of infectiousness. HBV DNA tests are used to measure the amount of HBV in the blood. If detectable, treatment for HBV is generally recommended.

Treatment

Fortunately, hepatitis B can be treated. In fact, some of the medications used to treat HIV are also the most effective treatments used for HBV. Tenofovir (Viread®), lamivudine (3TC), emtricitabine (FTC) and the combination of tenofovir/FTC (Truvada®) can all be used to reduce the HBV to undetectable levels, usually as part of a combination HIV treatment regimen. Other HBV drugs are also active against HIV, so they should only be used when HIV levels are undetectable. If HBV drugs are used without also receiving fully effective HIV treatment, there is a high risk that HIV will develop resistance. Controlling HBV to undetectable levels leads to reduced rates of liver disease and can prevent cirrhosis.

Vaccination

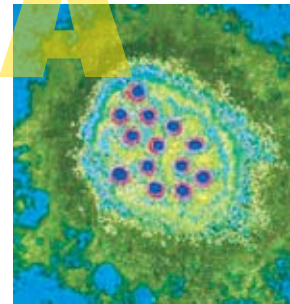
For those who haven't ever had hepatitis B (have negative antibody tests), vaccination is recommended, particularly for anyone who's chronically infected with HCV or has partners or family members with chronic HBV. HBV vaccination requires three shots of vaccine, given over a six-month period. Vaccination can be very effective at preventing HBV. However, not all people with HIV will respond well to vaccines, because their immune system may prevent the development of protective antibodies. It's therefore important to get HBV antibody levels measured following the vaccine series to make sure it worked.

Hepatitis C virus (HCV)

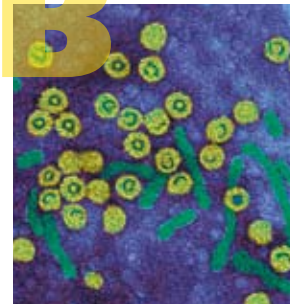
The most common chronic viral co-infection with HIV is HCV, which affects up to 30% of people living with HIV. HCV is mainly transmitted through blood transfusions, the sharing of injection drug use equipment and tattoos under non-sterile conditions. It can also, though less commonly, be transmitted

continued on page 12

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Dr. Marina B. Klein is Associate Professor of Medicine at the McGill University Health Centre, Division of Infectious Diseases and Immunodeficiency.

Resources

where to get the help you need

National resources

Canadian HIV/AIDS Legal Network

1240 Bay Street, Suite 600, Toronto,
Tel. (416) 595-1666
www.aidslaw.ca



Canadian Aboriginal AIDS Network (CAAN)

251 Bank Street, Suite 602, Ottawa
Tel. (613) 567-1817 (toll free: 1-888-285-2226)
www.caan.ca



Canadian AIDS Treatment Information Exchange (CATIE)

555 Richmond Street West, Suite 505,
Toronto (mail only)
Tel. (416) 203-7122 (toll free: 1-800-263-1638)
www.catie.ca



Canadian AIDS Society

190 O'Connor Street, Suite 800, Ottawa
Tel. (613) 230-3580
www.cdnaids.ca



Canadian Treatment Action Council (CTAC)

555 Richmond Street W, Suite 1109B, Toronto
(416) 410-6538
www.ctac.ca



Canadian Working Group on HIV & Rehabilitation

1240 Bay Street, Suite 600, Toronto
Tel. (416) 513-0440
www.hivandrehab.ca



Canadian HIV Trials Network

St. Paul's Hospital
620-1081 Burrard Street, Vancouver
Tel. (604) 806-8327 (toll free: 1-800-661-4664)
www.hivnet.ubc.ca/ctn



Education and support leaders on the HIV Prevention and Care team at The Group Health Centre (formerly AIDS Network of Sault Ste. Marie).

British Columbia

AIDS Vancouver

1107 Seymour Street, Vancouver
Tel. (604) 681-2201 (toll free: 1-800-994-2437)
www.aidsvancouver.org



British Columbia Persons with AIDS Society (BCWPAS)

1107 Seymour Street, 2nd Floor, Vancouver
Tel. (604) 893-2200 (toll free: 1-800-994-2437)
www.bcpwa.org



Positive Women's Network

1033 Davie Street, Suite 614, Vancouver
Tel. (604) 692-3000 (toll free: 1-866-692-3001)
www.pwn.bc.ca



Healing Our Spirit – B.C. Aboriginal HIV/AIDS Society

Suite 100 – 2425 Quebec Street, Suite 100, Vancouver
Tel. (604) 879-8884 (toll free: 1-800-336-9726)
www.healingourspirit.org



Youthco AIDS Society

900 Helmcken St, Vancouver
Tel. (604) 688-1441 (toll free: 1-877-Youthco)
www.youthco.org



ANKORS

101 Baker Street, Nelson
Tel. (250) 505-5506 (toll free: 1-800-421-2437)
www.ankors.bc.ca



AIDS Society of Kamloops (ASK)

437 Lansdowne Street, Kamloops
Tel. (250) 372-7585 (toll free: 1-800-661-7541)
www.aidskamloops.bc.ca



Victoria Persons with AIDS Society

1139 Yates St, Victoria
Tel. (250) 382-7927
www.vpwas.com



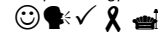
VARCS – Victoria AIDS Resource & Community Services Society

1284F Gladstone Avenue, Victoria
Tel. (250) 388-6220
www.varcs.org



Living Positive Resource Centre Okanagan (LPRC)

101 – 266 Lawrence Avenue, Kelowna
Tel. (250) 862-2437 (toll free: 1-800-616-2437)
<http://livingpositive.ca/>



Alberta

AIDS Calgary Awareness Association

110, 1603 10th ave. SW, Calgary
Tel. (403) 508-2500
<http://www.aidscalgary.org>



Lethbridge HIV Connection

1206 – 6th Avenue South, Lethbridge
Tel. (403) 328-8186
www.lethbridgehiv.com



Living Positive

10550 – 102 Street NW #100, Edmonton
Tel. (780) 488-5768 (toll free 1-877-975-9448)
www.edmlivingpositive.ca



HIV Edmonton – HIV Network of Edmonton Society

11456 Jasper Ave, Suite 300, Edmonton
Tel. (780) 488-5742
www.hivedmonton.com



HIV North Society

10116 102nd Ave, Grande Prairie
 Tel. (780) 538-3388
www.hivnorth.org

Central Alberta AIDS Network Society

4611 50th Avenue, Red Deer
 Tel. (403) 346-8868 (toll free: 1-877-346-8858)
www.mycommunityinformation.com/caans/

Saskatchewan

AIDS Programs South Saskatchewan (APSS)

2815 5th Avenue, Regina
 Tel. (306) 924-8420 (toll free: 1-877-210-7622)
www.aidsresourcesask.ca

PLWA Network of Saskatchewan

PO Box 7123, Saskatoon
 Tel. (306) 373-7766 (toll free: 1-800-226-0944)
www.sasktelwebsite.net/plwaid/

AIDS Saskatoon

130A Idylwyld Drive North, Saskatoon
 Tel. (306) 242-5005
www.aids Saskatoon.ca

Manitoba

Nine Circles Community Health Centre

705 Broadway, Winnipeg
 Tel. (204) 940-6000
www.ninecircles.ca/kalishivaaidsservices.htm

Rainbow Resource Centre

1 – 222 Osborne Street South, Winnipeg
 Tel. (204) 284-5208
www.mts.net/~rainbow8/

Ontario

Access AIDS Network Sault Ste Marie

167 Gore Street, Sault Ste. Marie
 Tel: (705) 256-2437

AIDS Niagara

111 Church Street, St. Catharines,
 Tel. (905) 984-8684 (toll free: 1-800-773-9843)
www.aidsniagara.com

Toronto PWA Foundation

399 Church Street, 2nd Floor, Toronto
 Tel. (416) 506-1400
www.pwatoronto.org

AIDS Committee of Toronto (ACT)

399 Church Street, 4th Floor, Toronto
 Tel. (416) 340-8484
www.actontario.org

Positive Youth Outreach

399 Church Street, 4th Floor, Toronto
 Tel. (416) 340-8484, x281 (toll free: 1-877-767-0688)
www.positiveyouth.com
 (For youth 13-29)

Alliance for South Asian AIDS Prevention

20 Carlton Street, Suite 126 (Floor M), Toronto
 Tel. (416) 599-2727
www.asaap.ca

Africans in Partnership Against AIDS (APAA)

110 Spadina Ave., Suite 207, Toronto
 Tel. (416) 924-5256
www.apaa.ca

AIDS Committee of Ottawa (ACO) / Comité sida d'Ottawa (CSO)

251 Bank Street, Suite 700, Ottawa
 Tel. (613) 238-5014
www.aco-cso.ca

AIDS Committee of North Bay and Area

269 Main Street West, Suite 201, North Bay
 Tel. (705) 497-3560
<http://aidsnorthbay.com>

Access AIDS Network Sudbury

111 Elm Street, Unit 203, Sudbury
 Tel: (705) 688-0500

Québec

COCQ-SIDA

1, rue Sherbrooke Est, Montréal
 Tel. (514) 844-2477
www.cocqsida.com

AIDS Community Care Montreal (ACCM)

2075 Plessis, Basement Level, Montréal
 Tel. (514) 527-0926
www.accmontreal.org

NCJW Chesed Direct Service Network

6900 Decarie Blvd, Suite 348, Montréal
 Tel. (514) 733-2589
www.generation.net/~chesed

I.R.I.S. Estrie

505 rue Wellington Sud, Sherbrooke
 Tel: (819) 823-6704
www.iris-estrie.com

New Brunswick

AIDS New Brunswick / SIDA Nouveau-Brunswick

65 Brunswick Street, Room G17,
 Victoria Health Centre, Fredericton
 Tel. (506) 459-7518 (toll free: 1-800-561-4009)
www.aidsnb.com

SIDA-AIDS Moncton

165A Gordon Street, Moncton
 Tel. (506) 859-9616
www.sida-aidsmoncton.com

Prince Edward Island

AIDS PEI

10 St. Peters Road, Charlottetown
 Tel. (902) 566-2437 (toll free: 1-800-314-2437)
www.aidspei.com

Nova Scotia

Northern AIDS Connection Society

33 Pleasant Street, Truro
 Tel. (902) 895-0931
<http://nacsns.tripod.com/>

AIDS Coalition of Nova Scotia

1657 Barrington Street, Suite 326, Halifax
 Tel. Local: (902) 425-4882 toll free: 1-800-566-2437
www.acns.ns.ca

Healing Our Nations

Atlantic First Nations AIDS Network

45 Alderney Drive, Suite # 607, Dartmouth
 Tel. (902) 492-4255 (toll free: 1-800-565-4255)
www.healingournations.ca

Newfoundland and Labrador

AIDS Committee of Newfoundland & Labrador

Suite 100 – 50 Harbour Drive, St. John's
 Tel. (709) 579-8656 (hotline: 1-800-563-1575)
www.acnl.net

Conception Bay North AIDS Interest Group

Taylor Building, Carbonear
 Tel. (709) 596-4433 (toll free: 1-877-596-4433)
www.cbnaig.org

There are more AIDS Service Organizations across Canada than we can hope to list on two pages. We try to rotate them so that most appear over four issues.

For a complete list, please see: www.catie.ca/eng/links/local.shtml

sexually, and from mother to child. Infection with HIV increases the risk for acquiring HCV sexually and in childbirth. Acute HCV has increasingly been seen in HIV-positive MSM engaging in high-risk sexual activities. HIV-HCV co-infection also occurs commonly in sub-Saharan Africa, Latin America and South-East Asia, so immigrants from these areas are at particular risk.

Infection with HCV results in an acute hepatitis, which tends to produce fewer symptoms than hepatitis A or B. Some people with acute HCV

of HCV somewhat, but HIV-HCV co-infected persons remain at high risk for liver-related complications despite treatment. In part, this may be because HIV treatments themselves can affect the liver. Other factors such as alcohol use, which accelerates liver disease in HCV, may also be important.

Diagnosis is made by testing for HCV antibodies in the blood. Chronic infection is diagnosed by detecting HCV virus (RNA) in blood. Liver biopsies are often performed to determine the amount of damage done to the liver and whether treatment is indicated.

There's no vaccine to protect against HCV. Prevention requires avoiding high-risk activities, particularly those related to the sharing of injection drug use equipment (not just needles, but spoons, straws and other "works"), and certain sexual activities.

Complex treatment

There's treatment available for HCV, but it's challenging to take and to tolerate, and it doesn't work in everyone. The standard HCV treatment is pegylated interferon-alpha 2a (Pegasys®) or alpha 2b (Pegetron®) — taken weekly by injection — combined with ribavirin taken orally twice daily. Recent studies suggest that there are no differences between the two available interferon products. Side effects often include flu-like symptoms, anemia, weight loss, fatigue and depression. Treatment is most effective when given during acute HCV, where up to 80% will be cured. In chronic infection, cure rates are lower and depend on the genotype, or strain, of HCV infection. The treatment response rate is about 40% on average in genotypes 1 and 4, and 60% to 70% in genotypes 2 and 3.

Despite the challenges associated with HCV treatment, it can be given successfully to a majority of people, especially in a centre that can provide multidisciplinary support. HCV treatment is the only intervention so far that's been clearly shown to improve outcomes for HIV-HCV co-infection, so it's important to be evaluated for treatment if you have HCV infection.

Avoid liver disease

An increasing number of people are chronically infected with HCV and/or HBV and HIV due to the shared routes of transmission. With the availability of effective HIV therapies, liver disease secondary to hepatitis co-infections has emerged as a leading cause of illness and death in people with HIV and may complicate HIV treatment. It's important to get tested, get vaccinated and get treated for these conditions to reduce your risk of liver disease. **R**

Testing for hepatitis

An antibody titre is a lab test that measures the presence in your blood of antibodies to viruses that cause hepatitis A, hepatitis B, or hepatitis C. The body creates antibodies to attack and remove foreign substances (like hepatitis virus), and the level of antibodies reflects past exposure to this substance. Elevated Immunoglobulin M (IgM) antibodies indicate acute hepatitis. Elevated Immunoglobulin G (IgG) antibodies suggest chronic hepatitis.

will clear the infection on their own, without any treatment. However, approximately 80% of those infected with HCV will go on to develop chronic infection, which, if untreated, may eventually lead to cirrhosis, liver failure and liver cancer.

Effects on HIV treatment

HCV doesn't appear to affect HIV, but can make it more difficult to tolerate HIV treatments. As with HBV, HIV makes HCV worse, leading to faster rates of liver disease, cirrhosis and death from liver-related causes. Treatment of HIV appears to slow the effects



Cosmetic treatment for lipodystrophy

A review of available options **by Dr. Yves Hébert**

Dr. Yves Hébert is a general practitioner who has worked in the field of aesthetic medicine for over 20 years. He provides a wide array of treatments at his Montreal-based clinic, and is an expert in the treatment of lipoatrophy. He is on the Board of the Canadian Association of Esthetic Medicine and, in July 2009, will become the president of the Association for a three-year mandate.

Lipodystrophy is among the complications people worry about most when they're treated for HIV, primarily because it can produce changes to the body that are visible to the outside world. While research continues on precisely how it's caused and how the benefits of antiretroviral

treatment can be delivered without risk of lipodystrophy, it may be reassuring to know that cosmetic options are available to reduce the changes in appearance.

Lipodystrophy affects a growing number of people on antiretroviral therapy. In 2008, it was estimated that, of the two million people infected with HIV in North America and Europe, some 285,000 suffered from lipodystrophy. That number is expected to climb to 380,000 by 2012!

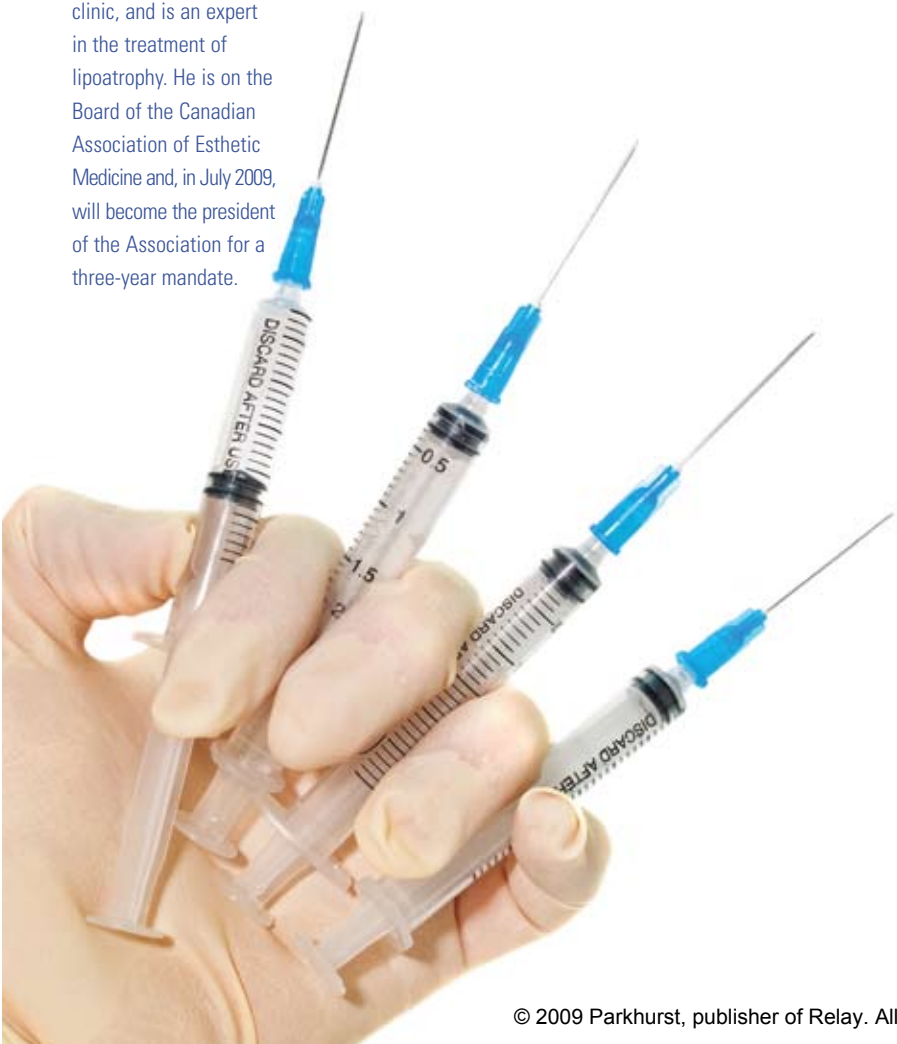
The word lipodystrophy literally means "fat (lipo) disorder (dystrophy)." It describes an abnormal change in the way the body metabolizes and distributes fat. Metabolism is how your body processes fats, sugars and some chemicals that are produced as it breaks down food. Distribution is where fat gets deposited under the skin around your body.

Changes in fat metabolism

Changes in metabolism can increase the levels of various types of fat (cholesterol and triglycerides) and sugar in your blood, and may lead to an increased risk of cardiovascular (heart) problems and a greater likelihood of diabetes. People living with HIV suffer heart attacks almost twice as often as people without HIV and have double the incidence of diabetes. (See "Heart disease and antiretroviral therapy" on page 7).

Changes in fat distribution

While metabolic abnormalities associated with lipodystrophy can compromise health, problems with fat distribution can have a negative impact on quality of life, as they lead to changes in appearance





Getting rid of abnormal fat deposits

Liposuction or surgical removal can be used to remove fatty deposits, especially the hump between the shoulder blades. Liposuction is generally performed under local anaesthetic, involves little discomfort or risk, leaves only tiny scars and doesn't require a hospital stay. Surgical removal is done under general anaesthetic and requires a brief stay in hospital. It leaves a scar several centimetres long near the top of the back between the shoulder blades.

Both approaches are effective at eliminating the hump or other deposits, but there's a risk of them coming back after a few years, especially if the same antiretroviral regimen is maintained.

Fillers for lipoatrophy

Cosmetic surgery can also help correct the effects of lipoatrophy in the face and return fullness to hollow cheeks and temples by injecting different forms of implant or filler material under the skin.

In theory, all injectable fillers approved by Health Canada and marketed here can be used to treat lipoatrophy. Fillers are commonly used to reduce the appearance of wrinkles and scars. However, some fillers, such as hyaluronic acid-based products (Perlane™, Juvederm™, Teosyal™, etc) and porcine

that many find difficult to cope with. Some people notice lipoaccumulation, where fatty tissue accumulates abnormally in the abdomen, between the shoulder blades (where it can build up into what's commonly called a buffalo hump), in the breasts, or as lipomas (small fatty lumps under the skin). Others may see a loss of fatty tissue, or lipoatrophy, in the buttocks, arms, legs and face. It's possible to experience both lipoaccumulation and lipoatrophy at the same time.

It can be disturbing to watch your appearance start to change and to lose control over the shape of your body. The hallmark sunken cheeks or buffalo hump also increase fears of discrimination, as people feel that their HIV is suddenly visible. Social isolation is a real risk if you start avoiding contact with others. The appearance of lipodystrophy scares some people into stopping their antiretroviral (ARV) regimens without really thinking through the consequences of doing so. In such instances, psychological distress is then compounded by the risk of worsening HIV infection and the development of resistance.

Treating lipodystrophy

While there are currently no proven strategies for reversing the metabolic changes associated with lipodystrophy, cosmetic surgery is being used successfully to reverse changes in fat distribution. Unfortunately, the treatments and procedures described below are considered "cosmetic" and aren't covered under public or private insurance plans, making it difficult for many Canadians to afford treatment.



collagen-based products (Evolve™) have short-lasting effects of between six months and one year, and are therefore not very cost-effective, despite being very safe to use. At best, they can help out with small superficial touch-ups.

Poly-lactic acid (Sculptra™)

This product, also known as NewFill™ in Europe, progressively fills in affected areas by stimulating collagen production and a gradual thickening of the skin. Depending on the severity of lipoatrophy, between three and six treatments, undertaken at intervals of four to eight weeks, may be required. Results last between two and three years and periodic maintenance treatments after that allow results to be maintained. The treatment is moderately painful and has a few side effects (swelling and bruising) that last only a short while. In rare cases, nodules can form under the skin, but these generally disappear with time. Its excellent safety profile makes Sculptra the treatment of choice for lipoatrophy.

Calcium hydroxylapatite (Radiesse™)

This product is made from microparticles of calcium that stimulate the formation of new collagen fibres, leading to a durable and natural filling. It lasts between one and a half and two years. Depending on the severity of lipoatrophy, the series of treatments can be performed at two- to three-month intervals, with occasional touch-ups after that to maintain volume. Treatment is moderately painful and may produce some short-lasting bruising and swelling. It's an attractive option for people with mild lipoatrophy.

Polyalkylimide (Bio-Alcamid™)

This is the only permanent filler currently available in Canada. It's a water-based gel that's injected deep under the skin until the desired volume is reached, usually in one or two treatment sessions. It behaves like a soft implant that fills the tissue by integrating with it completely. Treatment is done under local anaesthetic and involves more intense side effects than other treatments (swelling, bruising, sensitivity, hardening of the skin). These effects last several days and wear off gradually. For reasons we still don't understand, 2% to 3% of people can't tolerate this product and develop abscesses and inflammation. The only option should this happen is to gradually remove as much of the product as possible through small incisions in the skin.



Polymethyl methacrylate (PMMA) (Artecoll™, Artesense™)

With a life-span of five to 10 years, these are semi-permanent products composed of microscopic particles of PMMA (a plastic polymer) that stimulate collagen formation after they're injected. A series of treatments at three-month intervals is usually needed before the desired results are obtained. PMMA's prolonged durability means that touch-ups can be spaced several years apart. Treatment is only slightly painful and involves some temporary swelling and bruising. However, in some people, PMMA can, over the long term, produce nodules and inflammatory reactions that are difficult to treat.

Access and affordability

The products mentioned above can all be administered during an outpatient visit at a medical clinic, and (with the possible exception of Bio-Alcamid) shouldn't require you to take time off work. They're generally safe when administered by a competent doctor who has experience and training in the particularities of each product.

Injectable fillers are expensive and the total bill for a course of treatment can come to between a few hundred and a few thousand dollars. These costs aren't covered or reimbursed by the public provincial health systems or by private insurance plans. **R**



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because you asked

Triple therapy

Is it really necessary to take three different antiretrovirals?

Dr. Marianne Harris answers: With the antiretroviral agents available today, the answer is yes. Long-term control of HIV infection was first achieved in the mid-1990s with the advent of triple drug regimens, also known as highly active antiretroviral therapy (HAART). Earlier treatments consisting of one or two drugs were only partially effective for a short time, apparently because the HIV virus can rapidly develop resistance to one or two drugs. However, it's much more difficult for the virus to develop resistance to three drugs given together.

The widespread use of triple therapy over the last 12 years has resulted in significant improvements in the effectiveness and durability of HIV treatment. The sustained control of viral replication and increases in CD4 cell counts achieved with three-drug HAART ultimately translate into fewer AIDS-related illnesses and longer life expectancy for people living with HIV.

Of course, taking three drugs at a time can be inconvenient and cumbersome. One approach that has been studied to improve convenience and reduce pill burden is to start on a triple drug regimen to bring the HIV viral load under control, then simplify to a single drug for "maintenance" therapy. The monotherapy used most often in these studies is a protease inhibitor (PI) such as lopinavir/ritonavir (Kaletra®), a potent antiretroviral agent for which it's relatively difficult for HIV to develop resistance. However, a recent paper reviewed the results of 22 PI monotherapy studies and showed that the risk of treatment failure was greater on monotherapy (33%) than on traditional triple therapy (23%). So for the time being, triple therapy is the gold standard for HIV treatment.



Drug interactions

Are there drug interactions between antiretroviral medications (ARVs) and Alertec™ or Ritalin™?

Danielle Gourde answers: Modafinil is a medication sold by the name Provigil™ in the United States and as Alertec™ in Canada. The recognized indications for this medication are daytime hypersomnolence (extreme sleepiness) accompanied by narcolepsy (fits of sleepiness), or as treatment for daytime hypersomnolence secondary to sleep apnea (interrupted sleep due to breathing difficulties).

Interactions between ARVs and modafinil haven't been studied. However, we know that modafinil uses the same metabolic pathways as ARVs, particularly protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs), and could therefore affect ARV concentrations.

These interactions are only theoretical but could lead to a decrease in the effectiveness of ARVs, which isn't desirable.

As well, the concentration of modafinil and potential side effects could be increased.

Treatment with modafinil should be started at a lower dose, and a blood test to measure ARV concentrations is recommended two weeks after you start taking the drug.

Atomoxetine (Strattera™), a medication used for the same indications as modafinil, has the same potential for interaction with ARVs and similar precautions should be taken. Methylphenidate (Ritalin™) is a safer alternative, because it doesn't interact with ARVs.

These central nervous system stimulant medications have been described as "smart drugs" by the popular press, but should be used with caution by people with heart disease, psychosis, anxiety or liver failure. Side effects associated with this class of drugs include headache and nervousness. These medications require a doctor's prescription and Alertec™ isn't covered by all drug plans, notably the Québec drug insurance plan. **R**

Marianne Harris, MD, CCFP, is a family doctor who currently works with the AIDS Research Program at the Immunodeficiency Clinic in St. Paul's Hospital, Vancouver.

Danielle Gourde is a pharmacist at Martin Duquette's pharmacy in Montreal, which has developed an expertise in HIV/AIDS.

Is there something
you need to know?
Please send your questions to:
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in the news

The XVIth Conference on Retroviruses and Opportunistic Infections (CROI) took place in Montreal from February 8 to 11, 2009. Relay's Co-Editor-in-Chief **Dr. Harold Dion** was there and reports some of the highlights from the meeting.

Preventing transmission

In 2008, Swiss researchers suggested that people taking ARVs whose plasma viral load (viral load apparent on a blood test) had been undetectable for at least six months may not be at risk for transmitting HIV. The Swiss went so far as to suggest that these people didn't have to use condoms or practise safer sex in certain circumstances (if their adherence to treatment was good, they had no fever and no other sexually transmitted infections).

At the CROI conference this year, several studies came to somewhat different conclusions, finding that more than 5% of men who had an undetectable plasma viral load could still have a detectable viral load in their semen. This would suggest that even though ARVs significantly reduce the risk of transmission, a blood test showing undetectable viral load doesn't necessarily reduce the risk of transmission to zero. It's therefore recommended that people continue to take adequate precautions.



New treatments

Little research on new antiretroviral treatments was presented. However, two early-stage (Phase I) studies were presented on new "boosting" medications. Currently, protease inhibitors (PIs) are generally prescribed along with small doses of another PI, ritonavir. These small ritonavir doses aren't active against HIV themselves, but work to boost the levels of the other drugs. These new investigational medications could potentially play a role similar to ritonavir.

The first study looked at a medication called GS-9350, co-formulated in a new "quadruple" pill containing four medications: GS-9350, emtricitabine (Emtriva[®]), tenofovir (Viread[®]) and elvitegravir (a new integrase inhibitor). GS-9350 was shown to increase the concentration of elvitegravir in the blood to 11 times its initial level. The treatment was well tolerated in HIV negative volunteers and had no negative effect on lipid (fat) metabolism. This "quadruple pill" will now be put into a larger Phase II study, which will compare it to Atripla[®] (tenofovir, emtricitabine and efavirenz). If it performs well, it may become another viable single-pill, multi-drug treatment option.

The second study looked at the tolerability of a new compound called SPI-452 and its ability to boost different PIs. Different doses of the medication (25, 50, 100, 200, 400 and 600 mg) were compared to placebo (a sugar pill). The new treatment was found to be safe and well tolerated, and it significantly increased the blood levels of saquinavir (Invirase[®]), atazanavir (Reyataz[®]) and darunavir (Prezista[®]). Researchers concluded that this new PI booster was very promising, and will continue to develop it.

Update on metabolic effects

There were a great number of oral and poster presentations, reflecting the impressive amount of research going on around the world. While there were no major breakthroughs in terms of new treatments for HIV, we found out more about the controversy surrounding metabolic problems and antiretrovirals (ARVs). See Dr. Marek Smieja's article on page 7 of this issue for an update on this question. **R**

This report looks at only a small sample of the presentations at the XVIth annual CROI conference. You can find a complete list of abstracts on the conference web site: www.retroconference.org/2009.





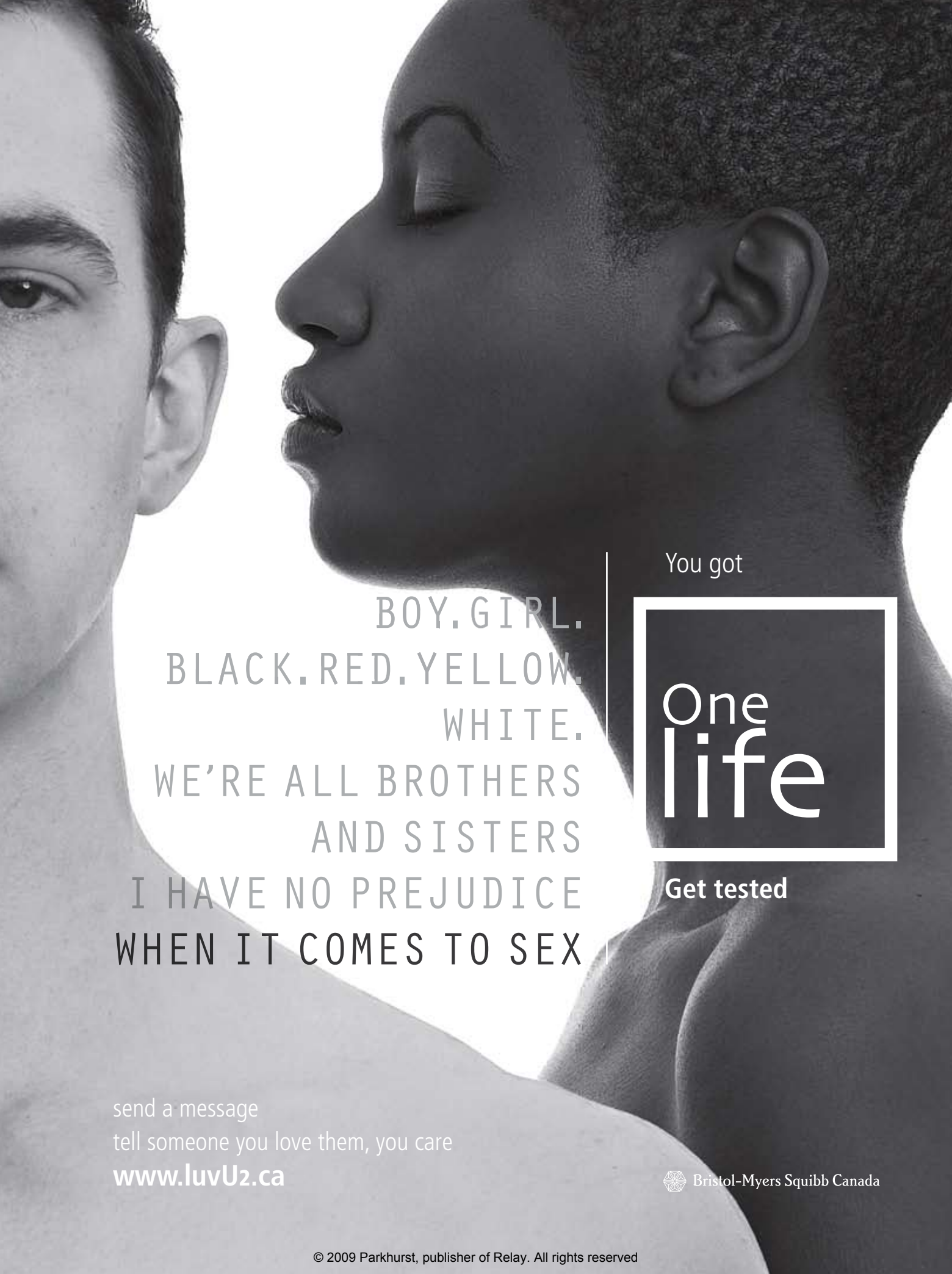
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