# Anal Cancer:

## *A Sexually Transmitted Disease*

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The incidence of anal cancer is similar in the U.S. and Canada; it occurs at a rate of approximately 1.3 to 1.4 per 100,000.[1,2] Rates increased between 1979 and 1996 and are currently higher in women than men.[1,3]

Death rates from anal cancer are about 0.2 per 100,000 and the five-year relative survival rates are 57 and 70 in males and females, respectively.[2] Anal cancer makes up only about 2.4% of all colorectal cancers.[1,4]

Anal cancer is much more common in certain subpopulations (Table 1).

Other groups that may be at increased risk of anal cancer include:

- women with concurrent high-grade cervical lesions or cervical cancer,
- women with high-grade vulvar intraepithelial neoplasia or vulvar cancer,
- other immunocompromised patients, and
- other HIV-infected patients (in addition to those who have had anal-receptive intercourse [ARI]).

### Jacob's case

Jacob, a 44-year-old heterosexual male, was noted to be HIV-positive in 1986. He had never had anal-receptive intercourse. The same year, he was diagnosed with non-Hodgkin's lymphoma and was successfully treated with chemotherapy.

In 1988, he had complicated cytomegalovirus retinitis and was left with reduced vision. He was treated with various antiretroviral regimens and, in 1996, went on highly active antiretroviral therapy. Since then, he had been very well, with CD4 counts > 400 cells/mm$^3$ and HIV viral loads of < 50 RNA copies/mL.

In 2000, he complained of anal discomfort and blood on the toilet paper. He was referred to an anorectal clinic, where he was examined several times over the year and was thought to have an anal fissure and anusitis.

In 2001, he had intense, persistent anal pain and some incontinence. He was seen by an anorectal surgeon, who performed a biopsy and found invasive squamous anal cancer involving the anal sphincter.

Jacob had an abdomino-perineal resection with permanent colostomy. He has remained in excellent general health with CD > 400 cells/mm$^3$ and an undetectable viral load.

**Table 1**

### Prevalence of anal cancer in specific subpopulations

| Subpopulation | Relative rate* |
|---|---|
| Males who have had ARI | 37-fold greater than the general population |
| Males under 30 who have had ARI | 163-fold greater than the general population |
| Men who have ARI and are also HIV-positive | Double the risk of those who have only had ARI |

**Despite the use of highly effective antiretroviral therapy, rates have been increasing during the HIV epidemic.*

ARI: Anal-receptive intercourse

Figure 1. High-resolution anoscopy. The mucosa is viewed through a colposcope. The image is stored digitally and is projected onto the video screen. The white lesion shown on this screen is high-grade precancerous dysplasia.

## HPV and anal cancer

Human papillomavirus is a very common virus with many subtypes, 40 of which infect the genital tract and are sexually transmitted. Cervical and anal cancers are associated with about 15 HPV types, called oncogenic types.

*In Canada, anal cancer occurs at a rate of 1.3 to 1.4 per 100,000; rates are currently higher in women.*

HPV is commonly acquired sexually, but carriage is usually transient and does not cause disease. Cancer is associated with persistence of carriage of HPV oncogenic types and may be more common in those who are immunocompromised and the elderly.

HPV can be detected by various tests, such as polymerase chain reaction or hybrid capture assay.

## Screening for anal cancer

There are several methods one can use to screen for precancerous anal lesions (dysplasia).

### 1. Look for the presence of oncogenic HPV

In the absence of oncogenic HPV, high-grade lesions or anal cancer should not occur. However, other types of HPV-associated lesions (*e.g.*, warts) can still occur, as these are caused by non-oncogenic HPV types. Unfortunately, HPV testing is not very useful in HIV-positive homosexual men because almost 100% carry HPV in the anal canal and about 90% have oncogenic HPV.

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**Table 2**

### Elements involved in establishing an anal cancer screening program

- Expert pathologists who are knowledgeable in diagnosing the relevant cytologic and histologic changes
- Personnel who are trained in high-resolution anoscopy, the treatment of dysplasia, and the performance of Pap smears.
- An anorectal surgeon
- An oncologist

## 2. Do a Pap smear

Similar to the detection of cervical cancer, the anal Pap smear is fairly easy to do; it is cheap, and standardized criteria are available for making pathologic diagnoses. The problem is the Pap smear has a fairly low sensitivity (30% to 50%), so internal lesions can be present even with a normal Pap result. Furthermore, the Pap is also not very specific; a cytologic abnormality on the Pap smear may not necessarily correlate exactly with the histologic abnormality present in the cervix or in the anal canal.

The advantage of the Pap smear is it can be repeated on a regular basis, which will improve its sensitivity for the detection of dysplasia.

## 3. Do high-resolution anoscopy

Currently the gold standard for the detection of dysplasia, high-resolution anoscopy involves viewing the squamocolumnar junction through an anoscope with the aid of a colposcope (which magnifies and illuminates the observed mucosa) (Figure 1). The anal canal can be stained with acetic acid and Lugol's iodine (to highlight any abnormalities suggesting dysplasia). Any visually abnormal areas must be biopsied to confirm the presence of dysplasia.

Using these techniques, high-grade dysplasia has been shown to occur at a prevalence of 25% to 30% in high-risk individuals. It is these dysplastic lesions that are

### *Frequently Asked Questions*

**1.** **Should warts in the anal canal be removed?**

Alone, warts are not cause for concern. They are usually caused by non-cancer producing types of HPV. If there is an indication of high-grade dysplasia (*e.g.*, on Pap smear), removing the warts might be useful for pathologic exam.

**2.** **It was discovered that a patient has HPV. What should be done? Should the patient wear a condom?**

HPV infection is extremely common and it's rare for cancer to develop. The best management would be to perform regular Pap smears to see if dysplasia is present. Always make the patient aware that HPV is sexually transmitted and the risk for acquiring new, and possibly dangerous forms of HPV increases with the number of partners. Condoms have not been proven to prevent HPV transmission.

**3.** **What is the relationship between circumcision and HPV?**

HPV penile infections are much less common in circumcised men. This results in protection against penile cancer, reduced transmission of HPV to sexual partners, and a marked reduction in risk of cervical cancer in female sexual partners.

most worrisome, as they may be the immediate precursors of anal cancer.

## What is the treatment for anal dysplasia?

Treatment options for anal dysplasia have not been standardized and tested for efficacy in preventing anal cancer. Some of the current options include:

- repeated applications of trichloroacetic acid, or
- the use of an infrared coagulator to ablate the dysplastic areas.

These techniques for lesion removal are more difficult and may not be as successful as for the treatment of cervical dysplasia, where larger areas of tissue can be removed.

In the anal canal, the aim is to remove the affected mucosa down to the basement membrane to remove all HPV-infected cells at the base of the lesion and around its full perimeter. This must be done without damaging the integrity and function of the anal canal.

## Take-home message

**How should you screen for anal cancer?**

- Look for the presence of oncogenic HPV.
- Pap smears can be used and are fairly easy to do. Although the Pap's sensitivity is relatively low, it can be improved by repeated testing.
- High-resolution anoscopy is the gold standard for the detection of dysplasia.

**What is the treatment for anal dysplasia?**

- Repeated applications of trichloroacetic acid.
- Infrared coagulator to ablate the dysplastic areas.

## Anal cancer screening programs

Anal cancer screening programs are quite uncommon; there are only a few sites in Canada that currently carry out this screening. It is recommended that, prior to establishing an anal cancer screening program, one must have all of the elements in place (Table 2). Just doing a Pap smear without all of these elements can cause a lot of confusion for the health-care providers and distress for the patient. Dx

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