

aids treatment update

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in this issue

This issue is dedicated to another sexually transmitted virus with a very similar name to HIV: human papilloma virus or HPV. This genital and anal wart virus is also associated with an increased risk of cervical and anal cancer. HIV-positive people are more likely than their HIV-negative counterparts to be diagnosed with HPV-related cancers.

HIV-positive women already benefit from regular cervical cancer screening. Before the national cervical Pap smear programme began in the 1960s, cervical cancer rates were about 40 per 100,000 women. It is now down to eight per 100,000. And HIV-positive women doing well on anti-HIV therapy who have regular cervical Pap smears now have similar rates of cervical cancer as their HIV-negative counterparts.

Screening for anal cancer is another story. At the moment, few HIV-positive men and women are being offered anal Pap smears. This may change very soon if the National Screening Committee decide to give anal Pap smears the go-ahead. This is a major opportunity for the UK to take the lead in preventing the third most common non-AIDS-defining cancer.

Even before the programme officially starts, you have the right to ask for an anal Pap smear. You could remind your HIV or GUM doctor, too, to consider including it in all their sexual health check-ups.

page 3 In *upfront*, we examine whether anal Pap smear tests are ready for prime time.

page 4 Discover ten things you should know about the wart virus.

page 6 Three doctors who specialise in both HIV and HPV-related cancer at London's Chelsea & Westminster Hospital, explain your cervical and anal cancer risks, share what they have learned about screening for anal cancer, and discuss current and future HPV treatments and vaccines.

page 10 Last year, after we included a request in *ATU* for personal contributions to NAM's book, *Living with HIV*, about the everyday issues of life with HIV, a young man wrote in and told us about his experiences with anal HPV. In this update, despite some of the best care in the country, he reveals that it hasn't been an easy ride.

page 12 Amongst the items in 'News in Brief', we discover that efavirenz (*Sustiva*) may linger much longer than previously thought when interrupting therapy, resulting in a high risk of resistance, and that even small CD4 rises when viral load is detectable can be good news.

page 15 Caspar Thomson, NAM's director, answers questions about *ATU's* recent relaunch and how NAM funds its treatments information work.



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anal pap smears

Is screening for anal cancer ready for prime time?

by Edwin J Bernard

Until recently, the idea of screening for anal cancer wasn't on anyone's radar. It wasn't very common, and it usually only affected people over 60. Does this sound familiar? This used to be the case with Kaposi's sarcoma before HIV came along. Then, during the 1990s, right after the introduction of HAART, cancer clinics in Europe and North America began seeing an increase in the number of younger people affected by anal cancer. It soon became apparent that HIV-positive gay men were being diagnosed in numbers far exceeding expectations and, unlike most other cancers, HAART wasn't making any difference to the numbers affected.

Studies suggested these gay men were living longer thanks to HAART, allowing time for their 'high-risk' HPV to become cancer. Other studies found that HIV-positive heterosexual male injecting drug users and HIV-positive women were also more likely than the general population to have anal pre-cancer, regardless of their sexual practices.

When pilot screening programmes began in San Francisco in the late 1990s, rates of anal pre-cancer were found to be higher than any incidence ever recorded in well-established cervical cancer screening programmes. This was when human rights activist Peter Tatchell began campaigning for the Department of Health to begin anal Pap smear screening for at-risk

individuals in the UK. Last year, after previous Ministers of Health had ignored or dismissed his campaign, "much to my surprise and delight, [Health Secretary] Dr John Reid referred my letter to the National Screening Committee," who decide which diseases should be screened for in the UK. "Within two weeks the Committee met and agreed 'the existing evidence should be reviewed and assessed', with a view to funding 'further research'. An evaluation project was started, led by Dr Muir Gray", Tatchell reflects.

On November 29th, the Committee will meet to decide whether screening for anal cancer is ready for prime time. "The evidence is good that there should be systematic testing for HIV-positive men and women," Dr Gray told the British HIV Association at their Autumn conference last month. He added, however, that the Committee needed to make sure that enough doctors in the UK know how to treat anal pre-cancer and cancer, because it is "unethical to offer people screening if treatment services are not adequate." Still, Dr Gray is at pains to point out that screening for any disease provides no guarantees: "Some of the people we'll find who'll have anal cancer would still die of anal cancer," he says.

Dr Paul Fox, who has been leading the pilot anal Pap smear programme at the Chelsea & Westminster, is hopeful. "There are a number of treatments emerging so it's not all bad news on the treatment front," he told the conference. "The UK really needs to take the lead in the world on this one: we actually have the opportunity to do this. We have the benefit of having a national health care system. The science of this condition is really only just developing and the momentum is beginning to increase, but we're very happy to admit that we don't have all the answers at this moment in time, but clearly that's not a reason not to look at it in much greater detail."

"It's early days yet," says Peter Tatchell, "but this looks like progress. The cancer that was once the object of shame and neglect is finally coming out of the closet."



HPV warts and all

Ten things HIV-positive men and women should know about the wart virus

What is HPV?

HPV stands for human papilloma virus which is also known as the genital wart virus. Papilloma is the medical term for a wart. So far, over 100 different strains, or genotypes, have been identified and new ones continue to be discovered on a yearly basis.

Which bodyparts does HPV affect?

Some of the non-sexually transmitted strains of HPV lead to warts on people's hands and feet, but these are different from genital warts and cross-infection is extremely rare.

In women, sexually transmitted HPV infects the cervix (the 'neck' of the womb at the top of the vagina) and the vulva (the external part of a woman's sexual organs).

In men, sexually transmitted HPV can infect the head, shaft and foreskin of the penis, and the scrotum.

In men and women, sexually transmitted HPV can infect the rectum (the last 20cm of the large intestine, just above the anus), the skin around the anus, and the area between the genitals and the anus (perianal region), whether or not you practice anal sex.

It can also, rarely, infect the mouth or throat of both men and women.



How do you get HPV?

HPV is very prevalent and is currently the second most frequently diagnosed sexually transmitted infection (STI) in the United Kingdom. Last year, around 80,000 people in the UK were diagnosed for the first time with genital warts, caused by some of the 30-40 HPV strains that are sexually transmitted.

HPV can be contracted during vaginal, oral or anal sex. It can also be transmitted through close physical contact. However, since it is the virus and not the wart that is infectious, and people can 'carry' HPV without having visible warts, warts don't have to be present for HPV to be transmitted. Condoms reduce the risk of HPV transmission and infection but do not completely prevent it. The more sexual partners you have, the more likely you are to be infected with one or more strains of HPV.

Many people are infected with at least one sexually transmitted HPV strain from the moment they become sexually active. Most infections are cleared spontaneously but a small proportion can persist, remaining with you for life.

Gay and bisexual men are twice as likely as heterosexuals to be diagnosed with genital warts, but HPV can affect all sexually active people, including lesbians.



What are the symptoms of HPV infection?

Genital warts are the only visible sign of HPV infection, but they may not appear for weeks, months or even years after infection occurs, if they appear at all. You may not realise you have warts, particularly if they are small, or inside the vagina or anus.

Warts may appear as small red or white bumps, they may grow alone or in cauliflower-like clusters, or they may be flat and barely visible.

Genital warts can occasionally cause irritation and discomfort, particularly during sex, although most cases are asymptomatic. It is the psychological and social effects of HPV infection, such as a sense of shame, depression, and anxiety, that represent the more significant toll for most people.

What diseases can HPV cause?

HPV-related diseases represent a spectrum from warts (usual) to cancer (relatively rare, but increasing, particularly in people with HIV) and can affect both men and women.

Some strains - most frequently HPV 6 & 11 - are associated with the raised kind of genital warts and are a low risk for cancer.

Others - most frequently HPV 16, 18 & 31 - are associated with a risk of developing cervical cancer in women, and anal cancer in both men and women. These strains have also been associated with penile, vaginal and vulval cancers. In addition, HPV is thought to play a role in the development of a number of other cancers, including those affecting the head and neck, the eyes, throat and possibly the skin.

However, being infected with a high-risk HPV strain does not necessarily mean that cancer will develop. Co-factors for the development of cancer are family history, smoking, increased age and immunosuppression. Regular screening for precancerous abnormalities can identify and treat those most at risk.

How does HIV affect HPV?

People with HIV tend to have a much harder time eliminating HPV, and keeping HPV under control. This means that if we have high-risk HPV, we have a much higher risk of cervical or anal cancer than the general population. But see also "How are HIV-positive women most frequently affected?".

Does anal HPV affect heterosexual men and women?

Sexually active HIV-positive heterosexual men and women are very likely to have anal HPV infection regardless of sexual behaviour. A French study from 2003 found that 46% of heterosexual male injection drug users who said they had never had anal sex had anal HPV infection^[6] and another US study found that about 75% of HIV-positive women had anal HPV infection, and that anal HPV infection was more frequent than cervical HPV infection^[7].



How are HIV-positive gay men most frequently affected?

Although everyone who is sexually active can be infected with HPV, HIV-positive gay men appear to be at the highest risk of HPV infection, particularly of anal HPV.

A recent study of HIV-positive gay men in San Francisco found that 95% of the men had anal HPV infection, and more than 50% had signs of precancerous lesions^[2].

In comparison, a recent study of HIV-negative men in four US cities found signs of precancerous lesions in 20%^[3].

HIV-positive gay men are also more likely to have multiple strains of HPV than HIV-negative gay men, increasing the likelihood of being infected with one or more of the high-risk strains.

How does HPV affect HIV?

Infection with one strain of HPV is now thought to double a person's risk of becoming infected with HIV, and infection with several strains more than triples the risk^[1].

How are HIV-positive women most frequently affected?

HIV-positive women are more likely than HIV-negative women to have cervical HPV infection. Last year, a large US study found that in comparison to HIV-negative women, HIV-positive women were three times more likely to have been infected with HPV. This study also found that HIV-positive women who smoked were about a third more likely to have any kind of HPV, and about twice as likely to have high-risk HPV strains than HIV-positive non-smokers^[4].

However, since screening for cervical cancer is recommended for all sexually active women, the same US study group found that the risk for cervical cancer now appears to be no higher for HIV-positive women on anti-HIV treatment and receiving regular screening and prevention than for their HIV-negative counterparts^[5].

Summary

- Sexually-transmitted HPV can lead to cancer.
- Cervical cancer is an AIDS-defining condition.
- HIV-positive women should be screened frequently.
- Anal cancer is relatively rare.
- Despite HAART, incidence of anal cancer is increasing.
- HIV-positive gay men are at highest risk, but everyone with HIV is at higher risk than the general population.
- Screening for anal cancer is possible and cost-effective, but few clinics offer it.
- Preventative and therapeutic HPV vaccines are on their way.

HPV-related diseases represent a spectrum from warts to cancer, affecting both men and women. Anal and cervical cancers are thought to share risk factors, causes and have similar biology. Moreover, both have an increasing incidence, particularly in individuals infected with HIV.

Invasive cervical cancer is believed to be the final stage in a continuum that starts with cervical infection by high-risk strains of human papillomavirus (HPV) and progresses via precancerous lesions, known as cervical intraepithelial neoplasia (CIN), to invasive cancer. CIN is diagnosed via a Pap smear and is divided into three grades (CIN 1-3).

The equivalent disease process for anal cancer begins with high-risk HPV infection and progresses through the three grades of precancerous lesions, known as anal intraepithelial neoplasia (AIN 1-3).

Cervical cancer

Invasive cervical cancer was included as an AIDS-defining diagnosis in 1993, although at the time the incidence of cervical cancer was not significantly increased in HIV-positive women. Today, there is good evidence that precancerous lesions occur more frequently in women with HIV^[1,2], although a recent study from the United States found that HIV-positive women who underwent regular

screening and prevention had a similar incidence of invasive cervical cancer as HIV-negative or untested women^[3].

In most UK hospitals HIV-positive women with invasive cervical cancer are given the same anticancer treatment as HIV-negative women. However, studies have found that HIV-positive women tend to have more advanced cervical cancer than their HIV-negative counterparts^[4], and that HIV-positive women with cervical cancer relapsed more frequently and tended not to survive as long as their HIV-negative counterparts^[5].

It is recommended, therefore, that cervical smears should be offered to all HIV-positive women more frequently than their HIV-negative counterparts, and that CIN should be aggressively treated in these women.

HAART, condoms and cervical cancer

Although there was hope that the survival of invasive cervical cancer may improve after the introduction of HAART, there are very few data to support this optimism^[6]. Although some studies have shown that HIV-positive women on HAART have improved outcomes, not all studies have found this to be true, and HAART appears to have



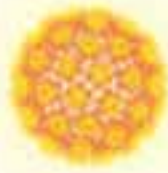
HPV & cancer

In this article especially written for *ATU*, three doctors who specialise in both HIV and HPV-related cancer at London's Chelsea & Westminster Hospital explain about cervical and anal cancer risks, share what they have learned about screening for anal cancer, and discuss new and forthcoming treatments and vaccines.

By Justin Stebbing, Rachel Lewis and Mark Bower

only limited ability to clear HPV infection and induce regression of CIN in HIV-positive women.

However, a Dutch study recently found that consistent condom use can hasten the regression of lesions in the cervix caused by high-risk HPV, and can speed up the time it takes the body to clear HPV infection. It is thought that the use of condoms prevented continued transmission of HPV between partners, leading to lower HPV viral load, preventing reinfection with HPV, and promoting quicker clearance of the virus^[7].



Anal cancer

Anal cancer is not an AIDS-defining illness. Fortunately, it is rare according to data from the largest single clinic HIV cohort in the UK at the Chelsea & Westminster, although the incidence is rising. A total of 26 cases of invasive anal cancer have been diagnosed here since 1986, 25 of them in gay men (the remaining case being in a heterosexual woman). If high-grade CIN is left untreated, then in over 30 years between 10 and 40% of patients will develop invasive cancer. The evidence for this is based on data from a single study of untreated patients with CIN carried out many years ago in New Zealand. In contrast, the natural history of AIN has not been

established, nor has the effect of treatment with HAART.

HAART and anal cancer

Several studies have found that incidence of anal cancer has not fallen with the introduction of HAART. We have also found that, since 1996, two thirds of individuals diagnosed with HIV-associated anal cancer at the Chelsea & Westminster were taking HAART, and one third had a viral load below 50 copies/ml. Moreover, the development of anal cancer is not linked to the severity of immune suppression: the median CD4 cell count of individuals presenting with anal cancer at the Chelsea & Westminster has been around 200 cells/mm³. We have also investigated the effect of starting HAART in 23 HIV-positive gay men with symptomatic AIN^[8]. Overall eight improved, ten remained stable and five worsened. However, none of the patients with the highest grade of precancerous lesions, AIN 3, progressed during twelve months of follow-up.

A recent study of HIV-positive gay men in San Francisco confirms our findings that HAART is not protective of AIN, and adds to the data that suggests that incidence of anal cancer is rising^[9].

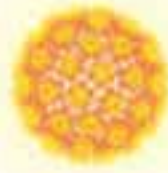
Screening for cervical cancer

Screening for cervical cancer began in the UK in 1964. Screening is based upon cervical (Pap) smear assessment and the current recommendation is for screening every three years, although

HIV-positive women should be screened more frequently. About four-and-a-half million women are screened annually in the UK and there has been a decline in the incidence of cervical cancer of around 40% over the last 20 years. Deaths from cervical cancer have also decreased dramatically, falling from 11.2 deaths per 100,000 women in 1950 to 3.3 in 1999. Screening for cervical cancer is considered to be cost-effective because screening detects the disease at an earlier stage, and earlier detection is associated with an improved outcome particularly when abnormal areas of the cervix are removed surgically. However, screening cannot catch all cervical cancers, and it can miss adenocarcinoma (cancer that begins in cells that line the inside of organs) and highly aggressive rapid cancer of the cervix.

Screening for anal cancer

There is currently no national anal cancer screening programme and many HIV centres wishing to offer screening are uncertain about how best to proceed. Anal Pap smears are a useful screening tool, but taking an anal smear poses more difficulties than taking a cervical smear, and there are very few trained anoscopists in the UK to whom patients with abnormal smear results might be referred for biopsies.



glossary

ablation
removal by laser.

anal intraepithelial neoplasia (AIN)
abnormal new growth of cells within the layer of cells that form the surface or lining of the anus.

anoscopy
a visual examination of the anal canal with an anoscope, a tube about 7.5cm in length with light attached at one end.

cauterisation
removal by burning.

cervical intraepithelial neoplasia (CIN)
abnormal new growth of cells within the layer of cells that form the surface or lining of the cervix.

chemotherapy
treatment with anticancer drugs.

cytological
relating to cytology, the examination of cells under a microscope using swabs or scrapings e.g. a Pap smear test.

efficacy
the ability to be effective.

excision
removal by cutting.

genotyping
the process of analysing particular genetic variations or strains.

HAART (highly active antiretroviral therapy)
a term used since 1996 to describe anti-HIV combination therapy with three or more drugs.

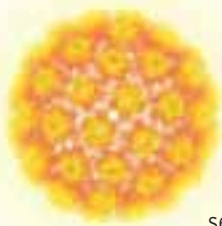
immunomodulatory
modifying or affecting the immune system.

invasive cancer
cancer that has spread to nearby tissue, lymph nodes under the arm, or other parts of the body.

Pap smear
a specimen of cells from the cervix, usually obtained in scrapings from the opening, which may be examined by microscope to look for abnormalities, named after its inventor, Dr George Nicolas Papanicolaou.

radiotherapy
treatment by radiation to kill cancer cells and shrink tumours.

An anoscopy clinic was established at the Chelsea & Westminster in September 2000. The target groups for screening were patients with unexplained anal symptoms, suspicious lesions in the anal canal, and those diagnosed with AIN following routine anal surgery. We demonstrated that anal Pap smears are simple to undertake, and that they have a sensitivity (82%) and specificity (45%) comparable with cervical Pap smears. We also found that HPV genotyping is not a useful addition to cytological screening. This suggests they can be used as the basis of pilot screening projects in centres with large cohorts of HIV-positive gay men who have a high risk of developing anal carcinoma^[10].



that anal warts have no significance and do not necessarily need to be treated. This has not helped gay men become aware of the potential seriousness of a lump in the anus.

It is hoped that a reduction in anal cancer incidence and improvements in survival similar to that of cervical cancer could be achieved with screening for anal cancer in at-risk populations, which includes all sexually active HIV-positive individuals, but in particular HIV-positive gay men. The detection of pre-invasive anal lesions and invasive anal cancer at early stages of disease might substantially improve survival.

Suggestions for future anal Pap smear programmes

We suggest that there is no compelling reason to treat low grade AIN, which should be monitored with annual Pap smears.

For small high grade AIN lesions that are few in number, excision or ablation might offer the prospect of a cure. This could be undertaken by the anoscopist without anaesthesia using trichloroacetic acid, or by excision or cauterisation in the operating theatre.

For large or multiple lesions such an approach is much more problematic, and the complications from surgical

treatments are high, with uncontrollable pain for three weeks post-procedure in half of the patients. This matters because the recurrence rate in HIV-positive patients is very high at 79% after an average of 28 months follow-up.

For large or multiple lesions we therefore propose monitoring with six-monthly anoscopy, which would enable any cancer to be identified at a relatively early stage, at which time local excision is followed by combined chemo- and radiotherapy.

This approach is clearly not ideal, but we hope that in the long-term more acceptable treatments will become available in form of topical, or immunomodulatory treatment or surgery.

Imiquimod

Imiquimod is a drug that stimulates the immune system to produce interferon alfa, a natural chemical which helps the body to fight viruses. The drug does not have direct antiviral activity, but it is thought to stimulate local immune activity against HPV, causing resolution of wart tissue and reduction of HPV viral burden. It has been approved in Europe and the United States for the treatment of warts, with the trade name *Aldara*. Imiquimod cream has shown good efficacy and safety in the

Anal cancer and survival

Currently, the overall survival at two years for patients with invasive anal cancer is 47%. Early intervention with a combination of chemotherapy and radiotherapy is associated with a better outcome, but the early detection of lesions poses substantial difficulties.

A significant problem at the Chelsea & Westminster has been the relatively advanced stage of anal cancer at the time of diagnosis. A commonly held belief within genitourinary medicine is

HPV in numbers

80,000

the number of people diagnosed with genital warts in the UK last year

95

the likely percentage of gay HIV-positive men infected with anal HPV

400

the approximate number of people diagnosed with anal cancer each year in the UK

16/18

the two HPV strains most commonly associated with cervical or anal cancer

75

the likely percentage of HIV-positive women infected with anal HPV

70-84


the estimated increased risk of anal cancer for HIV-positive gay men compared with the general population, i.e. 70 to 84 times higher

treatment of external genital and anal warts caused by HPV infection in both men and women. However, imiquimod cream can cause side-effects, including redness, swelling, hardening under the skin, wearing away of the top skin layers, blisters, ulcers, scabbing, pain, burning and itching.

A trial is currently underway at the Chelsea & Westminster to see if the cream is a safe and effective treatment for the treatment of AIN.

Is an HPV vaccine useful?

The successful development of preventative vaccines against HPV has recently been achieved and has been greeted with great enthusiasm.



Merck have studied 25,000 women using a vaccine against HPV types 6, 11, 16 and 18 and also studied 4,500 adolescents aged nine to 15. So far studies have demonstrated 98-100% efficacy at preventing persistent HPV infection, but they have not studied whether this means reduced cervical cancer incidence.

Glaxo Smith Kline (GSK) are approximately 18 months behind Merck, and have similar good results. Later this year, Merck will file a new drug application for their *Gardasil* vaccine with the US Food and Drug

Administration for a license to sell their vaccine, and it is thought that *Gardasil* will be available in the UK by the end of next year.

Merck and GSK hope to vaccinate all females between twelve and fourteen years of age.

Merck is currently studying *Gardasil* in 4,000 young men, including young gay men, and anal cancer is one of the study's endpoints. In addition, the US National Institutes of Health is studying *Gardasil* in preteen boys and girls with HIV.

Therapeutic HPV vaccines are also being developed to treat established HPV infections and HPV-associated cancers by targeting non-structural 'early' viral antigens of HPV, such as E6 and E7. If these therapeutic HPV vaccines prove as successful in patients as they have in animal models, HPV vaccines may one day have a role in the control of HPV infection and HPV-associated disease.

Conclusions

The HPV-associated cancers are emerging as a growing problem in people with HIV partly because HAART does not seem to prevent them, unlike Kaposi's sarcoma and non-Hodgkin's lymphoma. In the case of cervical cancer, pre-invasive disease

can be screened for and successfully treated surgically.

For anal cancer, pre-invasive disease can now be identified and screened for. The best management of these lesions is however not clear and ongoing surveillance is certainly warranted.

Although the introduction of prophylactic HPV vaccines is an exciting advance in medicine, they are likely to be of limited application in people who are already HIV-positive and infected with HPV, and we await eagerly the development of an effective treatment vaccine. ■

further information

For more information on HPV, and cervical and anal cancer risk for HIV-positive people, please visit www.aidsmap.com

The UK cancer charity, CancerBACUP provides detailed information about treatments for cervical and anal cancer on their website, www.cancerbacup.org.uk



37
the estimated increased risk of anal cancer for HIV-negative gay men compared with the general population, i.e. 37 times higher

3
the estimated increased risk for anal pre-cancer for HIV-positive women compared with HIV-negative women, i.e. 3 times higher

60
the average age at anal cancer diagnosis in the general population

40.9
the average age at anal cancer diagnosis in HIV-positive people

46
the likely percentage of heterosexual HIV-positive men infected with anal HPV

living with HPV

Last year, after we included a request in *ATU* for personal contributions to NAM's book, *Living with HIV*, about the everyday issues of life with HIV, a young man wrote in and told us about his experiences with *HPV*. He has very kindly provided an update for this issue of *ATU*, and, as you will read, despite some of the best care in the country, it hasn't been an easy ride.



My first bout of genital warts was uneventful. I came home from my first year at university with a self-diagnosis of piles - an unbearable itch in my back passage, and pain and blood after using the toilet. I came away from the GP with an instruction to visit a 'treatment centre' 20 miles away. After being quizzed about my sexual history, an examination revealed the presence of an anal fissure and a single anal wart. A quick blast of liquid nitrogen got rid of it.

Eight years later, a couple of years after an HIV diagnosis, the warts on my fingers, plus a few tiny ones on my chin, had returned and been removed with a quick nitrogen zap. When a subsequent examination revealed the presence of a few warts around my back passage, I assumed that a few icy blasts would see them off.

I followed my doctor's advice to pop into the clinic a couple of times a week to have the warts sprayed. I was encouraged by the nurses' reassurances that the warts were small and would soon be gone - especially as my viral load had plummeted from over 120,000 to below 50 copies/ml within a month of starting therapy.

As my visits started to stretch over weeks, then months, a trip back to my doctor revealed that the three months of cryotherapy had achieved nothing, probably on account of my sluggish CD4 count response: rather than climbing obediently, it had continued to fall before hovering around 130 for most of my first year on therapy.

In the two-month wait to be seen by a surgeon, the warts, no longer being kept in check by their regular liquid nitrogen fix or by imiquimod cream, grew to grotesque proportions. One grew inside my anal canal and prolapsed every time I used the toilet, eventually becoming more than 5cm in length and unbelievably painful. I felt disgusting and my sex drive evaporated.

I pinned my hopes on the operation. However, nothing (and no-one) had prepared me for how painful this would turn out to be. After three days in hospital on intravenous antibiotics,

there followed eight weeks of pain of a degree I had never imagined. I became terrified of using the toilet, necking laxatives and painkillers in handfuls and teetering on the edge of depression.

To top this off, the warts returned, even stronger, within a month of the surgery. On a return to see the surgeon, he nonchalantly informed me he "would have to repeat the procedure." Gritting my teeth through another three-month delay on a waiting list, the warts became larger than ever: I could barely walk for hours after using the toilet, and I was in tears most days.

Luckily, the second operation was far less traumatic than the first. I was up and ready to leave within hours of coming round, and felt better within days. I only had moderate pain for around a week and finally, after almost a year, I could use the toilet without fear.

However, the analysis of the tissue removed during this second procedure revealed that the condition had progressed from grade I to grade II/III pre-cancer in the four months between the two operations. All I could think about for the next few months was how I would cope with having cancer before I'd even turned 30 -

especially since my CD4 count was still low, getting stuck around 200, where it remains today.

I managed to allay some of my fears by encouraging my HIV doctor to refer me to Paul Fox at the Chelsea & Westminster Hospital. Dr Fox runs a weekly anoscopy clinic for gay men, where he takes samples of the anal tissue with Pap smears and examines the anal canal using an anoscope. The aim of this is to monitor the progression of the pre-cancer, and to catch the development of anal cancer early - in short, a similar procedure to cervical screening in women.

be part of the next edition of *living with hiv*

Do you have a story to tell about your experiences of HIV and living in the UK?

If so, please share them with us and they may be published in the next edition of *Living with HIV*.

You can submit them online at <http://www.aidsmap.com/livingwithhiv>, or email them to michael@nam.org.uk.



My first appointment was around six months after my second operation. Unfortunately, however, the examination revealed that the warts had grown back within my anus to such an extent that the doctor couldn't take a biopsy. I left, disappointed and scared, with an instruction to use imiquimod inside my anus for four months. Although it isn't a licensed treatment for internal use, he hoped that the cream would clear up the

warts so that he could take a proper sample of the underlying epithelium, where the pre-cancer is found. He likened the warts to trees in a forest, preventing him getting a good sample of the pre-cancer found in the 'ground' beneath the trees.

But things didn't go as smoothly as we hoped. A side-effect of imiquimod is local inflammation. At times over the next few months, this was so bad that I had sharp pains every time I went to the toilet. It also caused a mucous discharge from my back passage that led to intense chafing between my cheeks, making it difficult to walk at times. This was made worse by fungal infections on more than one occasion.

On top of that, the cream had no effect on the growth of the warts. Eighteen months after I first developed problems, I felt that I was back at square one, with prolapsing warts, pain on using the toilet and a growing feeling of desperation. Unsurprisingly, my return to see the anoscopy doctor led to a referral to a surgeon and after a (mercifully brief) delay, two more operations to remove the warts from inside my anus.

To my relief, there was no evidence of any pre-cancer in the tissue removed this time around, and, although I'm still recovering from the fourth operation, things look like they're getting back to normal - although I'll have to wait for another two months before I return for another anoscopy.

But I know I'm not out of the woods yet. The imiquimod cream is still causing irritation, and I'm well aware that the absence of any pre-cancer in the tissue the surgeons removed doesn't mean it's not lurking elsewhere. I also have developed a stenosis - a tightening of the anus caused by scar tissue from the four operations. This prevents the anus from opening properly, making it painful to open my bowels, or even insert a finger when I'm trying to apply the cream. I'm told this should ease with time and can be treated if necessary, but it's a

constant reminder that things aren't right down there.

I'm still worried about whether I might end up with cancer one of these days, or even that the warts will return and require more surgery. But what scares me the most is that the experts still don't know the best way to prevent progression from warts to pre-cancer to cancer - maybe they will have worked it out in ten years, but for me, right now, the uncertainty is difficult to deal with.

Overall, though, I'm feeling more positive since the pre-cancer wasn't found after my last operation. This has shown, to me at least, that HPV infection isn't a one-way process, even in someone with a low CD4 count - it can regress from pre-cancer back to plain warts as well as progress towards cancer. As for whether my pre-cancer will return, I'll just have to wait and see... ■

living with hiv

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This is an updated version of an article written for NAM's *Living with HIV* book.

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latest research

Efavirenz may linger for up to eight weeks after treatment stops

Levels of efavirenz (*Sustiva*) that are sufficient to cause drug resistance may linger for at least eight weeks after it is stopped in some people who have a genetic predisposition to clear the drug from the body very slowly, according to a new report. The report highlights the case of a UK woman of African ethnicity who suddenly stopped efavirenz treatment without telling her doctor because she feared that she was pregnant (efavirenz may cause birth defects if the foetus is exposed to the drug during the first 13 weeks of development). Remarkably, her viral load remained 'undetectable' eight weeks after stopping and did not rebound until twelve weeks after therapy ceased, by which time it had risen to 2031 copies/ml. A mutation associated with efavirenz resistance (M230L/M) was detectable at week 12, although the classic K103N mutation associated with efavirenz resistance did not emerge. The woman was found to have a liver enzyme mutation that is highly unusual in ethnically caucasian people. Although its frequency in people of African ethnicity is unknown, and its association with efavirenz clearance has not been established, a similar liver enzyme mutation is already known to be associated with slower efavirenz clearance in people of African ethnicity. The report's authors suggest that current UK recommendations to cover the efavirenz tail-off period with *Kaletra* for 14 days or to discontinue efavirenz 14 days before stopping other anti-HIV drugs may not be appropriate for everyone.



sexual health

Over 200 sexually transmitted LGV cases seen UK-wide

Two hundred and fifteen confirmed cases of the previously rare sexually transmitted infection, LGV (*lymphogranuloma venereum*), have now been confirmed in the United Kingdom. Cases have been reported throughout England, Scotland and Wales, although the majority have been diagnosed in London (153/215, 71%) and Brighton (31/215, 14%). The vast majority of LGV has been found in gay men who are chronically infected with HIV, although two cases have now been reported in heterosexual men. Most of the men were diagnosed after they had symptoms of proctitis, which includes rectal discharge, rectal pain and bloody stools. LGV can be treated with antibiotics, but only if diagnosed: some men have had symptoms for more than a year before diagnosis.



changing treatment

Detectable viral load? Even a small CD4 count increase is still good news

Even when your viral load isn't 'undetectable', as long as your CD4 count has increased by at least 25 cells/mm³ you will have substantially reduced your risk of HIV-related illness or death over the next year, according to a new study. Although the goal of anti-HIV therapy is to reduce viral load to 'undetectable' levels (usually less than 50 copies per millilitre of blood), some people, especially those who have previously taken anti-HIV therapy, don't manage this, but still manage to have CD4 increases. This is known as a 'discordant' treatment response. The study found

that each 25 cells/mm³ increase a year after starting the current therapy, even when viral load was detectable, reduced the chance of disease progression by 21%. The investigators suggest that their findings "have important implications for the management of antiretroviral-experienced patients" and recommend that if people with few treatment options have some CD4 count rises, however small, on their 'failing' anti-HIV regimen, they should stay on that 'failing' regimen until at least two drugs that are sensitive to their resistant HIV become available.

sexual health

Can an antibiotic tablet cure HIV-positive syphilis?

A new study has found that a single oral 2 gram dose of azithromycin (*Zithromax*) provides treatment for early and latent syphilis that is equivalent to a single injection of penicillin G benzathine (*Crystapen*). More than 50% of the people in the study were HIV-positive and the investigators found that azithromycin and penicillin worked equally well in HIV-positive individuals, with comparable cure rates achieved at three (60% versus 66%), six (81% versus 81%) and nine (94% versus 95%) months. However, the investigators did not obtain samples of cerebrospinal fluid to see whether the syphilis had affected the brain and spinal cord, known as neurosyphilis. Some UK doctors are concerned that HIV-positive patients are at increased risk of neurosyphilis. In fact, the British Association of Sexual Health and HIV (BASHH) recommend HIV-positive people with syphilis endure 17-21 consecutive days of *Jenacillin A* injections rather than the standard penicillin injection. Nevertheless, some UK clinics do provide this standard single injection to their HIV-positive patients.

the new hiv news update from nam

news from *hiv weekly*

HIV disease progression

French research has found that in the first few years of infection with HIV, factors that can cause stress are associated with illness, even if a person is taking anti-HIV drugs. The study involved 319 people and was conducted between 1996 and 2002. The aim was to see if there was a link between social and economic factors and the risk of hospitalisation or death during the first few years of HIV infection. Most people in the study were European men, and the majority became HIV-positive after having had sex with another man. Over two-thirds started taking anti-HIV therapy soon after their diagnosis with HIV, and by the end of the study, 80% were taking anti-HIV treatment.

Health factors which could increase the risk of illness were present in few of the patients.

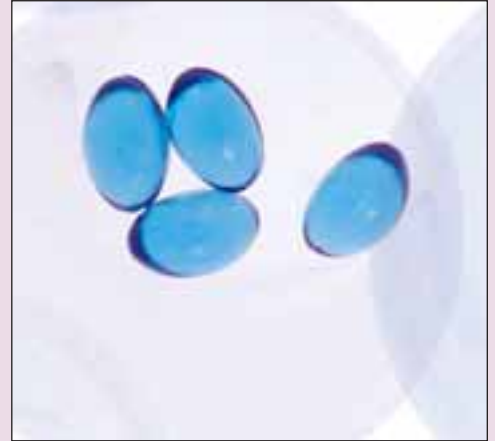
Only 5% were infected with hepatitis B or hepatitis C, 3% had lung disease, 2% had diabetes and 2% had mental health problems. A total of 89 people were hospitalised and three died. HIV or the side-effects of anti-HIV treatment caused 25% of hospitalisations, 21% were caused by mental health problems and the rest were due to causes such as surgery and non-HIV related causes. The three deaths were due to suicide, tuberculosis, and lymphoma.

Not having a stable job and not having a relationship were found to be risk factors for illness. The researchers believe that this could be because they caused stress, which as well as suppressing the immune system could also act as a trigger for smoking and drug use which could damage health.

subscribe to *hiv weekly*

NAM has launched a new, weekly email bulletin, *HIV Weekly*, that provides people affected by HIV with a concise, plain English digest of the very latest HIV news. The bulletin is edited by Michael Carter, NAM's patient information and news editor. One of the unique benefits of *HIV Weekly* is the inclusion of hyperlinks within the stories so that you can quickly and easily access further information on NAM's website, aidsmap.com, with the click of a mouse. Information and news about the latest NAM treatment information resources will also be included in the bulletin.

To receive your free weekly news digest visit www.aidsmap.com/hivweekly



salvage therapy

No interruption benefit for those with few treatment options

A new French study called REVERSE has found that people with very advanced HIV disease who have run out of treatment options don't benefit from an eight week treatment interruption. It was hoped that interrupting treatment for these people would make their multiple drug-resistant HIV disappear. Although this did happen to some of the participants, drug-resistant HIV returned soon after they restarted anti-HIV treatment. In fact, most of the study participants continued to lose CD4 cells and get sick after restarting treatment. These findings contradict the results of a controversial previous French study, GIGHAART, which found the eight week treatment interruption did help those with very few treatment options, as long as they restarted an average of six anti-HIV drugs. Despite these findings the study's investigators argue that short-term treatment interruption should be tested if the subsequent salvage regimen contains drugs assumed to be highly potent in salvage therapy, such as T-20 (enfuvirtide, *Fuzeon*), tipranavir (*Aptivus*), and the experimental protease inhibitor, TMC114.



news from nam

■ nam forum

NAM's November forum is for and about people newly diagnosed with HIV, providing information on all aspects of healthcare, and how to make sense of life with HIV. This will be the last NAM forum of 2005.

For those who have not yet attended a NAM forum, and can get to London, this a great way to acquire important new information about HIV from HIV doctors and other people living with HIV in a friendly, open atmosphere. Everyone is welcome, and refreshments are provided.

The forum will take place on Monday 28th November, between 7-9pm at the University of London Union, Rooms 3C & D, Third Floor, Malet Street, London, WC1. Questions from the audience are welcome, and to make sure your voice is heard you can even email your questions

in advance to forums@nam.org.uk. Visit www.aidsmap.com/en/events/forums.asp closer to the event for the most up-to-date details of who will be speaking at this event.




■ share the knowledge

If this issue of *AIDS Treatment Update* includes information which you think might be useful for a friend, family member or colleague, please do share it with them. Better still, why not encourage them to subscribe themselves? *ATU* is available free to individuals in the UK affected by HIV/AIDS by filling in the form on the back, calling 020 7840 0050, or emailing info@nam.org.uk.

■ correction

In last month's 'Starting Treatment' drug table, photos of *Kivexa* and *Truvada* were reversed. The pills actually look like this:

Table 2 BHIVA-Recommendations

Drug Name	
Choose Either One of these Fixed Dose Combinations	
	<i>Combivir</i> (300mg AZT/150mg ZDV)
	<i>Kivexa</i> (600mg abacavir, 300mg lamivudine)
	<i>Truvada</i> (300mg tenofovir, 200mg emtricitabine)

The corrected version of the drug table is now freely available as a pdf download at: www.aidsmap.com/atu

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HPV warts and all [page four]

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Over 200 sexually transmitted LGV cases seen UK-wide

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Funding NAM's treatments information

Caspar Thomson,
NAM's director,
answers questions
about ATU's
relaunch and how
NAM funds its
treatments
information work

Who was involved in the research that culminated in the ATU relaunch this month?

We were most fortunate that one of the country's leading qualitative researchers, John Rose, agreed to work with us on this project. John helped direct the research and guided us through the whole process, including providing training to key staff so they could undertake effective evaluation interviews. This meant we were able to keep the bulk of the work in-house, which helped to reduce the costs. I must also extend my thanks to all those readers who participated in the research and to those agencies that hosted the interviews. Your help has been invaluable in reshaping *ATU*.

Was it expensive to add more pages and full colour ATU?

Print technology has developed considerably since *ATU* was first launched in 1992. The processes involved in colour printing have evolved to such an extent that its cost has reduced dramatically, meaning there are barely any advantages from printing in just two colours. Because this new version of *ATU* has more pages, the cost of each print run has indeed increased, but only marginally. We decided that this small additional cost was more than worthwhile in order to make the newsletter more accessible, thereby reaching more people living with HIV.

Where do the funds come from to support the newsletter?

We couldn't have embarked on this exercise without the support and encouragement of the staff and trustees of the Elton John AIDS Foundation and the Derek Butler Trust, to whom we are very grateful indeed. Their generous contributions have enabled us to take all the necessary steps to ensure that we were making careful and informed decisions about the direction of the relaunch. We receive some further support towards the costs of publishing *ATU* from the Inner London HIV Commissioning Consortium, a number of Primary Care Trusts across England, and from several pharmaceutical companies, which give unrestricted grants towards NAM's wider treatments education programme. Lastly, but by no means least, during the past eighteen months quite a number of *ATU*'s subscribers have made donations towards the costs of publishing and distributing *ATU*, and of promoting the newsletter amongst key groups of people affected by the virus. Thank you to all of you.

Do any of your funders have any influence over what you write?

Independence, accuracy and impartiality are absolutely central to all of NAM's resources and they are standards we would never compromise. We have built our reputation upon these qualities and it is why we are such a trusted source of high quality information on HIV. This is where the support from the Elton John AIDS Foundation and the Derek Butler Trust is so critical. It enables us to retain an arm's-length relationship with the pharmaceutical companies and this helps us to sustain our independence at all times. Of course, we are very grateful indeed to the companies that contribute to our treatments education programme (which includes *ATU*, our monthly forums, patient information booklets, factsheets, directories, and our website, aidsmap.com). Their support is long-standing and has provided security in a rapidly changing funding environment. The grants they provide are, though, towards the wider education programme (allowing us to spread the funds across our various resources as we see fit) and there is no question of their being able to interfere with our editorial stance or influence us in any other way that undermines our independence. The companies understand, and have been good at honouring, our position on this.

How can individuals help support NAM?

We'd be delighted if you were able to support our work. We distribute *ATU* free of charge to anyone living with HIV and, of course, as more and more people subscribe the costs of this mount. With this relaunch we're hoping that subscriptions will climb, so any help you might be able to give us would be enormously welcome. If you would like to contribute simply call us on 020 7840 0050. We'll be very happy to take your call. ■



thanks to our funders

NAM's treatments information for people living with HIV is provided free thanks to the generosity of:

Abbott Laboratories International & UK; Access 4; Ajahma Charitable Trust; Alan & Nesta Ferguson Charitable Settlement; Birmingham PCT; The Body Shop Foundation; Boehringer Ingelheim International & UK; Bolton PCT; Bristol-Myers Squibb UK HIV & Hepatitis; British HIV Association (BHIVA); Cleopatra Trust; Corkery Group; Crusaid; Derek Butler Trust; Diana, Princess of Wales Memorial Fund; Government of the United Kingdom, Department of Health; East Sussex, Brighton & Hove area PCTs; Gilead International & UK; GlaxoSmithKline UK; Healthsure Charitable Trust; Hugh Fraser Foundation; International HIV/AIDS Alliance; Janssen-Cilag; Lloyds TSB Foundation for England and Wales; Lloyds TSB Foundation for Northern Ireland; London HIV & GUM Commissioning Consortium; MAC AIDS Fund; Merck Sharp & Dohme UK & International; Newcastle PCT; Norfolk PCT; Manchester city area PCTs; Miss Agnes H Hunter's Trust; Merton Social Services; Peter Moores Foundation; Pfizer UK & International; Positive Action (GSK); Roche Products UK Hep C; Roche Products International & UK; The Russell Trust; Salford PCT; Shire Pharmaceuticals; South East Essex PCTs; South West Essex PCTs; St. Stephen's AIDS Trust; Stockport Social Services; Thomas Sivewright Catto Charitable Settlement; Tibotec; Virco; West Sussex PCTs; Worcestershire PCT

NAM would also like to acknowledge the generous support of individual donors, and in particular Gavin Hay and Tim Cohen

Where to find out more about HIV

■ Find out more about HIV treatment:

NAM's factsheets, booklets, directories and website, keep you up to date about key topics, and are designed to help you make your healthcare and HIV treatment decisions. Contact NAM to find out more and order your copies.

■ Information events in London

On the last Monday of every month, an expert speaker discusses an HIV treatment related topic. Entry is free, further details are listed in this copy of *ATU*.

■ www.aidsmap.com

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