TreatmentUpdate 248

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Contents

I SEXUALLY TRANSMITTED INFECTIONS

A. Previous syphilis not linked to brain injury in Ontario HIV study

Before effective HIV treatment (ART) was available, people with HIV had weakened immune systems. As a result, they could develop injury to the brain or surrounding tissue and serious infections caused by several microbes. HIV itself could affect the brain and cause problems with memory and thinking clearly. In extreme cases, HIV-related brain-injury could lead to changes in personality.

Another issue that could result in brain injury was neurosyphilis. This occurs when the germs that cause syphilis (treponemes) spread to the brain.

Effective HIV treatment first became available in 1996. When taken as directed, ART helps to suppress levels of HIV in the blood and continued treatment keeps it suppressed. This suppression of HIV allows the immune system to begin to repair itself. The power of ART is so profound that researchers expect that many ART users will have near-normal life expectancy.

Syphilis and the brain

A team of researchers in Ontario wanted to investigate the impact of previous syphilis on assessments of memory, speed of thinking, learning, information processing and other higher cognitive functions in people with HIV in the current era. Tests that explore these cognitive functions are called neuropsychological testing.

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The researchers analyzed data collected from 1,288 people with HIV who underwent neuropsychological assessments. The researchers also analyzed information in participants' medical records, paying particular attention to data from 271 people who had diagnoses of syphilis.

The researchers found no relationship between a diagnosis of syphilis and any impact on neuropsychological testing. Note that past episodes of syphilis in participants were treated.

Although not the focus of the study, researchers found that nearly 40% of participants had depression. This condition can affect memory and clear thinking, so researchers took this into account when analyzing their results. Their finding of such a large proportion of people with depression also points to the importance of screening people with HIV for mental health issues and offering treatment when necessary.

The present study underscores the importance of initiating and taking ART, as well as the screening and treatment of syphilis.

About syphilis

Syphilis is a disease caused by the germ *Treponema pallidum*. Syphilis can be spread via sex and sharing equipment used for injecting drugs. Initial infection with T. pallidum can cause a painless sore or lesion in or on the genitals, anus, mouth or throat. This sore or lesion may be unnoticed particularly if it is inside the body. Shortly after infection, the germs that cause syphilis spread and can infect the eyes, brain, bones, heart and blood vessels, liver, kidneys and other vital organs. Syphilis can also affect the fetus during pregnancy. Syphilis can cause a wide array of symptoms that may initially be mild or mimic other conditions. The good news is that syphilis can be uncovered with a simple blood test and most people can be cured with a course of treatment. However, people can become reinfected with syphilis in the future (through the routes previously mentioned), so regular syphilis testing is important.

Study details

A brief average profile of the 1,288 participants when they entered the study is as follows:

- age – 44 years
- major ethno-racial groups: White – 54%; Black – 26%
- depression diagnosed – 37%
- taking ART – 81%
- drug use – 18%; researchers defined drug use as taking any of the following in the past six months – methamphetamine, cocaine/crack, opioids, tranquilizers and "club drugs"
- lowest-ever CD4+ count – 190 cells/mm3
- current CD4+ count – 450 cells/mm3
- time since first syphilis diagnosis – 3.4 years
- number of episodes of syphilis: none – 83%; one – 14%; two or more – 3%

Data were collected between January 2008 and December 2017. Researchers focused their analysis on 271 people who were diagnosed with syphilis.

On average, participants were in the study for two years.

Results

During the study there were 366 episodes of syphilis among 271 people.

Researchers found no impact of a history of syphilis on neuropsychological assessments.

Focus on neurosyphilis

During the study, 23 people were diagnosed with neurosyphilis.

Researchers noted that people who were diagnosed with neurosyphilis were more likely to have the following factors than people without neurosyphilis:

- used drugs in the past six months – 60% vs. 27% (the researchers did not publish information about how drugs were administered)
- a detectable viral load (more than 50 copies/mL) – 60% vs. 31%
- a longer duration of HIV infection – 12 years vs. 5 years

Despite these differences, researchers did not find any impact of a history of neurosyphilis on neuropsychological testing.

Bear in mind

Historically, neurosyphilis appeared to be more common among some people with HIV in the time before ART was available. What's more, neurosyphilis was associated with a range of brain complications among people with HIV in the pre-ART era. However, the present study did not find that syphilis had a significant impact on the functioning of the brain. The researchers advanced several possible reasons for this, as follows:

- Depression had a greater impact on cognitive function than syphilis, and depression was common among study participants.
- It is possible that people with problems with memory and thinking clearly caused by syphilis did not participate in the study.
- Neuropsychological assessments for this study took about 30 minutes to complete. More extensive assessments lasting two hours could have been done. Such assessments could have found subtle changes caused by syphilis (or other factors). However, it may be difficult to recruit and retain people for a study if more time consuming and complex assessments were used.
- During the study period more effective HIV treatments (a group of drugs called integrase inhibitors) were introduced and regimens were simplified. Such changes may have led to better control of HIV (via easier adherence) and a stronger immune system.
- More people could have initiated ART earlier in the course of HIV infection, and this could have preserved their neurocognitive functions. The researchers stated that people in the study "had generally good neurocognitive functioning overall (though less than population norms)."
- The researchers stated that any impact of syphilis on brain health "may be dwarfed by the benefit of modern ART."
- People in the study were relatively young; results may be different in older people.
- Due to frequent screening, syphilis in the study population may have been quickly uncovered by doctors and nurses and promptly treated. These factors may have minimized any neurological injury caused by syphilis.

Depression and sexually transmitted infections (STIs)

As mentioned earlier, a large proportion of people in the study had depression. The researchers noted that previous research has found a link between depression and newly diagnosed STIs. They stated that their finding (about high rates of depression) underscores the importance of screening study participants for mental health conditions when conducting studies of neurocognitive function in the future.

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II CANCER

A. Dutch HIV study finds implementing anal cancer screening and treatment saves lives

Some strains of human papillomavirus (HPV) are sexually transmitted and can cause abnormal development of cells in the following places:

- anus
- cervix
- lips
- mouth and/or throat
- penis
- vulva

In some cases, abnormal cells can eventually transform into pre-cancer and cancer.

Due to persistent HPV infection and a degree of immunological weakness, people with HIV as a group are at heightened risk for HPV-related abnormal cellular development and cancer. For this population, regular screening to detect pre-cancer and cancer of the affected body parts mentioned is needed.

A team of researchers in the Netherlands has conducted a study monitoring the health of more than 28,000 people with HIV. The study collected

data from 1996 to 2020. In that country, screening programs for anal pre-cancer and cancer were gradually expanded beginning in 2007. People in the program who had pre-cancer or cancer are referred for treatment.

In their most recent analysis, researchers found that over the course of the study 227 new cases of anal cancer were diagnosed. Over time, rates of anal cancer among a subgroup in the study—men who have sex with men (MSM)—fell, though the risk of anal cancer remained higher than in HIV-negative people. Furthermore, among MSM who underwent anal cancer screening, when anal cancer was diagnosed it tended to be found in the early stages before multiple tumours had appeared and spread. Deaths due to complications from anal cancer occurred in 4% of men who were screened vs. 24% of men who had not been screened.

The results from the Netherlands support programs for people with HIV that offer screening for anal pre-cancer/cancer and treatment when it is found.

Study details

A study called Athena enrolled many people with HIV from 28 clinics across the Netherlands.

In December 2007, anal cancer screening using high-resolution anoscopy (HRA) was gradually made available for people with HIV. As part of that screening, abnormal cells found in the anus were biopsied. If pre-cancer or cancer was found, treatment was offered (surgery, radiation and/or chemotherapy). Most people targeted for screening in the study were MSM.

In general, screening was offered every two years. However, if abnormal cells were detected, screening could occur more often. After treatment for pre-cancer/cancer, people were reassessed six months later to be sure that treatment was effective.

During the study period, 28,175 people with HIV were enrolled. They were divided into the following groups; note that gender at birth was used and sexual orientation was provided by participants. As such, MSM may include trans women and non-binary people:

- MSM – 60%
- non-MSM – 22%
- women – 19%

Note that numbers here and elsewhere in this report may not total 100 due to rounding.

During the study, 227 cases of anal cancer were diagnosed. Here is a brief average profile of participants at the time this cancer was diagnosed:

- age – 52 years
- time since HIV diagnosis – 14 years
- current CD4+ cell count – 480 cells/mm3
- lowest-ever CD4+ count – 110 cells/mm3
- 74% had an undetectable viral load (in this case, less than 40 copies/mL)
- time on ART – 10 years
- 13% of participants were in the anal cancer screening program at the time this cancer was diagnosed

Analysis of anal tumours revealed that the vast majority (99%) were squamous cell carcinoma.

Results

Over time, the risk of anal cancer fell significantly among MSM but not among other populations. This is noteworthy because MSM would have been aging and the immune system's ability to detect and destroy pre-cancers and cancers decreases with age as the immune system slowly degrades.

To explore why the risk for anal cancer decreased among MSM relative to other groups, the researchers conducted further analyses. They found that MSM as a group tended to have the following:

- less likely to smoke over time; that is, as new participants entered the study they were less likely to be smokers and people who entered the study as smokers were more likely to quit
- less likely to have had low CD4+ cell counts and high viral loads, probably due to earlier initiation of ART
- less likely to have viral loads greater than 1,000 copies thanks to initiation of ART and good adherence

Screening

During the study, 14% of all participants were screened at least once for anal cancer.

Of the 227 people diagnosed with anal cancer, 81% (184 people) had never been screened and were distributed as follows:

- MSM – 142
- non-MSM – 34
- women – 8

People who were screened were more likely to have been diagnosed with anal cancer. This should not be misconstrued as screening having caused cancer. Rather, doctors were actively looking for such cancers so they were more likely to be found in people who were screened.

Furthermore, such screening would be more likely to uncover anal cancer early in the course of disease compared to people who did not undergo screening.

Survival

Among 227 people diagnosed with anal cancer, 38% ultimately died. A total of 31% of deaths (from any cause) occurred within five years of diagnosis of anal cancer, distributed as follows:

- MSM – 31%
- non-MSM – 38%
- women – 63%

In general, there were more tumours found at the time of diagnosis of anal cancer among non-MSM than among MSM.

When researchers analyzed the deaths within five years of diagnosis, they found a connection between screening and survival:

- 4% of people who had undergone anal cancer screening and who had been diagnosed with anal cancer died from complications associated with anal cancer
- 24% of people who had *not* undergone anal cancer screening and who had been diagnosed with anal cancer died from complications associated with anal cancer

This difference underscores the impact and importance of screening.

Bear in mind

The Dutch researchers stated that new cases of anal cancer in MSM peaked in 2004 and then slowly decreased. However, the risk of this cancer occurring is still relatively high in this population.

The researchers stated that the decrease in anal cancer risk among MSM was driven by decreased rates of smoking and early initiation of ART. Minimizing the time with low CD4+ counts and high viral loads was found to reduce people's subsequent anal cancer risk.

People in the anal cancer screening program were more likely to have been diagnosed early with this cancer vs. people who were not in the screening program and who developed anal cancer. What's more, people in the screening program were much less likely to die from anal cancer–related complications than people who were not screened.

The Dutch study found that anal cancer risk is elevated in some non-MSM and women with HIV compared to people without HIV. Researchers found that this was not due to poor responses to ART. Some researchers in the Netherlands suspect that part of the reason for the elevated risk of anal cancer among some non-MSM might be due to what they described as "undisclosed sexual contact with other men."

For the future

The widespread use of ART has greatly increased life expectancy. However, as ART users grow older, they require monitoring so that any health issues are detected and treated early.

In the present study, anal cancer screening saved lives. Such screening needs to be more available to people with HIV in other countries. Research is needed to find out which subset of people with HIV are most in need of such screening.

Resources

Canadian Cancer Society

Cancer – Government of Canada

Cancer – Government of Quebec

Second cancer risk after surviving Hodgkin's lymphoma in people with HIV – *CATIE News*

French researchers investigate second cancers in people with HIV who survived a first cancer – *CATIE News*

Ontario study looks at trends in cancer in people with HIV – *CATIE News*

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B. Yale University study finds head and neck cancer linked to poor survival in people with HIV

Studies have found that people with HIV are at heightened risk for head and neck cancer. These cancers consist of tumours that can occur on the lips, mouth, throat and voice box; less commonly, the sinuses can be involved. Risk factors for head and neck cancers can include excessive sunlight (affecting the lips), use of alcohol and tobacco, and co-infection with viruses such as human papillomavirus (HPV) and Epstein-Barr Virus (EBV).

Chemicals in tobacco smoke and other substances, as well as HPV or EBV infection, can cause some cells lining the parts of the body previously mentioned to develop abnormally. Over time, some of these cells return to a normal development pathway. However, some cells may continue to develop abnormally, ultimately going on to become pre-cancer and cancer.

Ideally, cells of the immune system are supposed to patrol tissues and be on the lookout for pre-cancerous and cancerous cells. Upon finding these cells, patrolling cells of the immune system usually destroy them.

Despite the use of HIV treatment (ART), some degree of immunological dysfunction persists and pre-cancers and cancers may form.

The vaccine Gardasil-9 greatly reduces the risk of HPV-related cancers. However, this vaccine needs to be given when people are relatively young and have had no or few sexual partners. Many older people with HIV never had the opportunity to get the HPV vaccine when they were younger.

A vaccine to reduce the risk of EBV-related complications is under development.

At Yale University

A team of researchers at Yale New Haven Hospital conducted a study of head and neck cancers by reviewing data collected between 2002 and 2018 from people with and without HIV.

They found that after a diagnosis of head and/or neck cancer (hereafter simply called cancer), people with HIV had reduced survival (three years) vs. people without HIV with the same cancer (eight years). Sociodemographic and other factors could not explain the reduction in survival. Instead, statistical analysis pointed to something related to HIV.

It may be that the immune systems of people with HIV in this study were not functioning at an optimal level. It is also possible that there were unmeasured factors that the Yale University scientists missed when analysing the data.

The Yale researchers called for larger studies to confirm their findings. They also stated that people with HIV who have cancer should be offered more opportunities to participate in clinical trials exploring the use of drugs that help harness the anti-cancer activity of the immune system.

Study details

The Yale researchers accessed databases that collected information from people with cancer who sought care at the university's clinic. Researchers matched data from each person with HIV with data from at least three other people without HIV of the same gender, age, cancer, stage of cancer and location of cancer at the time of cancer diagnosis.

There were 2,894 people without HIV and 48 people with HIV in the study.

Small samples of tumours were analyzed for the presence of proteins from HPV.

The average profile of the HIV-positive participants at the time their cancer was diagnosed was as follows:

- 55 years
- 36 males, 12 females
- major ethno-racial groups – Black – 44%; White – 42%; Hispanic – 7%
- current or former tobacco use – 89%
- current or former alcohol use – 75%
- currently using ART – 88%
- viral load – 20 copies/mL; six people had a viral load greater than 200 copies/mL
- CD4+ count – 341 cells/mm3
- lowest-ever CD4+ count – 270 cells/mm3
- CD4/CD8 ratio – 0.5
- length of time since HIV diagnosis – 16 years
- co-infected with hepatitis C virus (HCV) – 66%

Results

There were important similarities between people with and without HIV. For instance, the researchers found the following:

- the locations of tumours were similar (usually the mouth and/or throat)
- the time between cancer diagnosis and initiation of anti-cancer treatment was similar
- the type of anti-cancer therapy prescribed was similar

After diagnosis, the overall survival of participants was distributed as follows:

- people with HIV – 34 months
- people without HIV – 94 months

When researchers focused only on people with a minimal number and size of tumours, they found improved survival among people with HIV (74 months), but it was still less than people without HIV (114 months).

Regardless of which timepoint after diagnosis researchers examined (two, eight and 10 years), HIV-positive people always had reduced survival compared to HIV-negative people.

Spurred by these findings, the study team performed statistical analyses hoping to uncover some factor(s) that might account for reduced survival among people with HIV. They were able to rule out the following factors measured at the time cancer was diagnosed:

- current CD4+ count
- current viral load
- age
- stage of cancer
- socio-economic factors
- tobacco use
- type of health insurance

A problem with the immune system

Cells of the immune system have an important role in dealing with abnormal cells, particularly tumours. One important group of cells is called CD8+ cells. This is a group of T-cells that can kill virus-infected cells and tumours. The researchers analysed samples of tumours taken from participants. They found that there were fewer CD8+ cells in the samples taken from people with HIV compared to samples taken from people without HIV.

In general, the researchers reported that people with HIV developed cancer at a significantly younger age (55 years) than people without HIV (62 years). This is striking because, in general, as people age, their immune systems become gradually weaker, increasing their risk for cancer.

This finding of the low number of CD8+ T-cells in tumours combined with the younger age at which people with HIV were diagnosed with cancer caused the researchers to argue that a major issue was the presence of HIV. This virus was having an effect on the immune system of people diagnosed with cancer.

HIV infection causes chronic immune activation and inflammation. This is greatly reduced with the use of ART and achievement and maintenance of a suppressed viral load. However, the levels of immune activation and inflammation still remain elevated compared to people without HIV. Some scientists think that prolonged exposure to excess immune activation and inflammation can slowly degrade the immune system. This does not mean that all or even most people with HIV will get cancer. However, research suggests that

ongoing immune activation and inflammation have the potential to increase the *risk* for cancer and contribute to an increased likelihood for the following issues:

- cardiovascular disease
- type 2 diabetes
- chronic kidney disease
- non-alcoholic fatty liver disease
- conditions where the immune system attacks the body (such as arthritis)
- neurodegenerative disorders

Bear in mind

The research from Yale University is a good first step at exploring the impact of HIV on the survival of people with cancer. Other studies have found that people with HIV are at heightened risk for cancer in the current era. This does not mean that most people with HIV will get cancer, but it does mean that their overall *risk* for cancer is increased.

The Yale study was relatively small and it is possible that some underlying drivers of poorer survival among people with HIV were not captured.

The Yale researchers need to cooperate with other cancer scientists to build a larger data set (with many more participants) to confirm their findings. Such a study will be expensive and will take years to accomplish, and the researchers will have to compete for scarce research funds.

Resources

Canadian Cancer Society

Cancer – Government of Canada

Cancer – Government of Quebec

Second cancer risk after surviving Hodgkin's lymphoma in people with HIV – *CATIE News*

French researchers investigate second cancers in people with HIV who survived a first cancer – *CATIE News*

Ontario study looks at trends in cancer in people with HIV – *CATIE News*

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C. The need to improve access to cancer clinical trials of immune checkpoint inhibitors for people with HIV

Immune-based therapy

Cancer cells release chemical signals that can weaken the immune system and its ability to sense and attack tumours. For more than a decade, pharmaceutical companies have been developing a class of cancer treatments called immune checkpoint inhibitors. These drugs work by removing restraints (checkpoints) on the immune system that can become more common when tumours develop. In theory, removing these checkpoints should help to unleash the immune system's natural ability to detect and attack tumours.

Examples of selected checkpoint inhibitors include the following:

- Keytruda (pembrolizumab) – this affects a molecule called PD-1
- Opdivo (nivolumab) – this affects a molecule called PD-1
- Yervoy (ipilibumab) – this affects a molecule called CTLA-4

In some clinical trials of people without HIV who have cancer, checkpoint inhibitors have produced remarkable anti-cancer effects. However, many

industry-sponsored trials have generally excluded people with HIV from large cancer clinical trials. Indeed, an analysis done by cancer specialists at Harvard University found that of "809 trials analyzed from 2019 to 2020, [nearly 75%] excluded […] people with HIV." The Harvard researchers stated: "Despite increasing evidence for safe and effective immune checkpoint inhibitor use for people with HIV, most cancer immune checkpoint inhibitor trials exclude people with HIV and few studies permit [such people] to participate, even if HIV is well controlled."

A small study done by researchers at the U.S. National Cancer Institute (NCI) focused on 87 designs for clinical trials (protocols) that were planned between 2014 and 2020. This study examined protocols that were planned for immune checkpoint inhibitors. The NCI study found that initially most protocols for the trials (84%) had no plans to recruit people with HIV who had cancer. But, after advocacy by the Cancer Therapy Evaluation Program of the NCI, protocols were changed and about 70% of the protocols then stated that people with HIV with cancer could enroll.

However, according to the same researchers at the NCI, the revised protocols then appeared to place barriers on the recruitment of people with HIV. The various barriers included having a minimum CD4+ count of 500 cells/mm^3, not being allowed to use antibiotics to prevent any infections, and, in some cases, excluding anyone who had ever had an AIDS-related infection regardless of their current CD4+ count. Follow-up research is needed to assess how many people with HIV subsequently were able to enroll in clinical trials of immune checkpoint inhibitors in these modified protocols.

At any rate, readers can see why doctors do not have large databases from which they can draw firm conclusions about the effects of immune checkpoint inhibitors on the cancers of people with HIV.

To remedy this situation, it would be helpful if the pharmaceutical industry and research institutes could facilitate trials of immune checkpoint inhibitors in people with HIV who have cancer so that doctors can gain experience with these drugs in this population.

For the future

Since 1996, effective HIV treatment (ART) has been amazingly transformational in Canada and other high-income countries. ART has turned an inevitably fatal viral infection into a chronic, manageable disease with a near-normal life expectancy for most people who take the medications as directed. If the life-prolonging effects of ART are to be fully realized, people with HIV who have cancer should have similar survival rates to people without HIV who have the same cancer. Perhaps equitable access to cancer therapy that works by harnessing the immune system is one possible approach to help people with HIV who have cancer and whose doctors judge such therapies to be needed.

Resources

Canadian Cancer Society

Cancer – Government of Canada

Cancer – Government of Quebec

Second cancer risk after surviving Hodgkin's lymphoma in people with HIV – *CATIE News*

French researchers investigate second cancers in people with HIV who survived a first cancer – *CATIE News*

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III SLEEP

A. Large U.S. study finds sleep-disordered breathing more common in men with HIV

Some people develop difficulty breathing during sleep. That is, their breathing becomes intermittent and can stop for a time. When they wake up, people with sleep-disordered breathing (sleep apnea) can feel tired, lack energy, be irritable and may experience drowsiness during the daytime.

Persistent sleep apnea causes the body's tissues to have insufficient oxygen. This can reduce the performance of the brain and muscles. Sleep apnea can also affect people's ability to work or volunteer and safely drive a motor vehicle, and it can degrade quality of life.

Emerging research suggests that sleep apnea can contribute to the following issues:

- high blood pressure
- cardiovascular disease
- abnormal blood sugar levels
- depression

People with sleep apnea may not be aware that they have it. For this and other reasons, people with unexplained and persistent generalized ill health or bothersome symptoms such as fatigue and sleeping problems should speak to their doctor or nurse for advice rather than make assumptions about the cause of their symptoms.

In general, risk factors for sleep apnea can include the following:

- male gender
- obesity
- post-menopausal status
- abnormalities in the structure of the throat or nasal passages

A common treatment

After a diagnosis of sleep apnea, doctors can present treatment options. The most commonly used option is a machine that provides continuous positive airway pressure (CPAP). One end of a flexible light hose is connected to a CPAP machine with the other end connected to a mask or nosepiece. The hose delivers room air at a constant pressure and the mask or nosepiece helps to direct the air to the lungs. CPAP machines help people with sleep apnea breathe while sleeping. From time to time, adjustments to the airflow and mask may be needed and sleep clinic staff can advise about this.

Sleep apnea and HIV

There have not been large studies to assess the occurrence of sleep apnea in people with HIV. To begin to explore this issue, a team of researchers at several universities in the U.S. conducted a study, called the Multicenter AIDS Cohort Study (MACS), with more than 800 men—466 with HIV and 370 without HIV. Participants had their sleep assessed with sensors overnight.

The researchers found that sleep apnea was common—around 50% overall. Men with HIV were more likely to have sleep apnea than men without HIV (56% vs. 48%).

Researchers applied extensive statistical analysis to try to find possible risk factors that could explain why sleep apnea was more common among men with HIV. However, they did not find any significant risk factors.

The researchers encouraged doctors and nurses caring for men with HIV to screen them for possible sleep apnea (when warranted), as this disorder can affect health and quality of life.

Study details

Researchers taught participants how to apply the different sensors that would be needed to assess sleep-disordered breathing so that participants could do the study in their own bedrooms. Participants received access to videos and print materials that explained how to apply the sensors. Data were collected electronically by a portable recording device loaned to participants. Sleep was assessed one time (overnight). Participants applied sensors to their head (to record brain waves and eye movements), chest (to record heart rate and breathing) and a finger (to assess the amount of oxygen in their blood). Small, soft flexible tubes were placed near the nose to assess the flow of air into the nostrils.

All participants were gay or bisexual men. The average profile of HIV-positive men when they entered the sleep study was as follows:

- age – 55 years
- body mass index (BMI) – 27.2 kg/m2
- major ethno-racial groups – White – 57%; Black 32%
- CD4+ count – 702 cells/mm3
- 94% of men had a suppressed viral load (the researchers defined this as being less than 200 copies/mL)
- 99% of men were taking HIV treatment; most commonly a regimen based on integrase inhibitors (47%)

The study took place between March 2018 through June 2019.

Results

Using a strict definition of sleep-disordered breathing, researchers found that sleep apnea was more common among men with HIV (56%) than men without HIV (48%).

Men with HIV were more likely to report daytime sleepiness than men without HIV.

Most men with HIV had sleep apnea that was either rated as mild or moderate by the researchers.

Why the difference?

Researchers undertook extensive statistical analyses to try to uncover possible risk factors that could have made men with HIV more vulnerable to developing sleep apnea than men without HIV. They considered factors such as age, race/ethnicity and BMI.

A similar analysis was done specifically among men with HIV, comparing those who had a detectable viral load (36 men) with those who had an undetectable viral load (430 men).

None of these statistical analyses yielded any fruitful information.

Bear in mind

So far, MACS is the largest study to assess sleep apnea in men with HIV. The researchers encouraged healthcare providers to screen men with HIV for sleep apnea.

Like all studies, the MACS sleep study is imperfect; its findings may not apply to all men living with HIV today. Historically, MACS has conducted many important studies. It first began enrolling men in what researchers called "waves of recruitment" in the following periods:

- 1984 to 1985
- 1987 to 1991
- 2001 to 2003
- 2010 to 2017

As a result, it is possible that some of the men who participated in the sleep study were there in part because of survivor bias. That is, they had some factor(s) that enabled them to survive in the time before HIV treatment (ART) was widely available so that they were alive today. Some of these men may also have spent years with a detectable viral load in the pre-ART era. This could have affected

their health and, possibly, their subsequent risk for sleep apnea.

Note that over the past decade doctors have increasingly moved to initiate ART soon after a diagnosis of HIV is made in order to minimize injury to the immune system (and other key organ-systems) that can occur with prolonged exposure to high levels of HIV.

For the future

More research is needed to uncover the drivers of sleep apnea in men with HIV. Also, research needs to be done with women who have HIV.

Note well

Persistent sleep problems, fatigue and irritability can have many potential causes. These problems are best discussed with a doctor so that they can help uncover the cause(s).

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Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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CATIE is Canada's source for up-to-date, unbiased information about HIV and hepatitis C. We connect people living with HIV or hepatitis C, at-risk communities, healthcare providers and community organizations with the knowledge, resources and expertise to reduce transmission and improve quality of life.

For more than 20 years, CATIE has been there to provide information that enables people to make informed choices about their health and enhances the ability of healthcare providers and other frontline organizations to respond to their clients' needs.

CATIE provides such information through a comprehensive website (www.catie.ca), electronic and print resources, webinars and other online learning, a national reference library, regional conferences, subscriptions to e-newsletters and a confidential phone inquiry service.

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