I INFECTION FIGHTERS

A. LGV: An old infection resurges

Uncommon in the past decade, a sexually transmitted disease called LGV (lymphogranuloma venereum) has reappeared in Western Europe, the United States and, now, according to anecdotal reports from several physicians, Canada as well. All the cases so far have been among gay or bisexual men, many of whom are also HIV positive.

The current outbreak of this bacterial infection appears to have begun in 2003 in the Netherlands. Initially, some cases of LGV may have been confused with other conditions such as inflammatory bowel disease. This may have happened because nowadays this infection is relatively uncommon and, in the current outbreak, symptoms of LGV were somewhat different from what they were in the past. However, as more cases emerged, doctors made the correct diagnosis with the help of sophisticated laboratory testing.

In this issue of Treatment Update we present findings from doctors in the Netherlands, where there is an outbreak of LGV, with about 100 cases now being reported. We also summarize key features of the infection as well as its treatment. In the age of hi-tech tests such as PCR (polymerase chain reaction) and effective treatments for LGV, many questions about the current outbreak need to be answered. We highlight future directions for LGV research.

B. When germs travel

Before antibiotics became widely available, outbreaks of the bacterial infection LGV, caused by several strains of Chlamydia, appeared regularly in the United States and Western Europe. Once
When antibiotics became available, the few cases that did occur were thought to be imported from regions where LGV infection continues to cause problems, such as:

- East and West Africa
- India
- Southeast Asia
- Central and South America
- parts of the Caribbean, such as the Bahamas

However, beginning in February 2003, three HIV positive men sought medical help at an STD clinic in Rotterdam, the Netherlands, because of symptoms of a possible infection. These three men helped researchers contact other men (with whom they had previously had sex). In an average year, the Netherlands usually has only a handful of cases of LGV, so as the size of the outbreak became clear, these cases triggered an investigation. The Rotterdam team focused on the 14 initial cases and here’s what they found:

- 11 of the 14 men were HIV positive.
- Four of the men were taking highly active antiretroviral therapy (HAART).
- In half of the 14 cases there was another sexually transmitted disease (STD) present, including rectal gonorrhea, genital herpes, syphilis, hepatitis B, genital warts.
- All of the men were white and lived in the Netherlands, particularly in Amsterdam or Rotterdam.
- The average age of the men was 39 years.
- Most of the men had had more than 10 sexual partners in the previous six months.
- All 14 men had engaged in anal sex.
- 10 of the men reported that they had engaged in regular fisting.
- Condom use was very limited, with about half of the men reporting that they never used them and the other half reporting that they used them some of the time.

### Symptoms

Among 12 of the men, the most common problems for which they sought help were as follows:

- a creamy discharge consisting of mucus and pus from the anus
- constipation
- rectal bleeding

Less common symptoms included the following:

- a constant need to empty the bowel, accompanied by pain, cramping and straining
- involuntary weight loss

None of the men reported having swollen lymph nodes in the groin. This is important because historically LGV infection is associated with swollen lymph nodes in that part of the body.

### Scoping around

Doctors found ulcers inside the rectums of all the men. PCR tests revealed that Chlamydia was present in almost all biopsies of the rectum. Further analyses revealed that in most cases the men had strains of Chlamydia that were called L₁, L₂ and L₃—the cause of LGV.

### Treatment

All the men with confirmed or suspected LGV were treated with antibiotics:

- doxycycline, 100 mg twice daily for 21 days

Fortunately, they all recovered from LGV infection. If left untreated, LGV can cause scarring of the colon and possibly bursting of lymph nodes in the groin.

The research team suspects that these men are merely a small part of a much larger outbreak that is appearing across Western Europe. This is because many of the men had a number of sexual contacts, most of whom were anonymous partners who cannot be contacted and warned that they, too, might have LGV. The 14 men in the study were part of an international sex network, meeting, as the researchers put it, on the “leather scene,” and therefore, not surprisingly, further outbreaks of LGV have appeared in the following places:

- Belgium
- France
- Germany
- Spain
- Sweden
- United Kingdom

In addition, reports from New York City and San Francisco indicate that cases of LGV are being investigated there. Several cases of LGV are also being investigated by public health authorities in Ontario and Western Canada.

Because LGV is associated with ulcers and bleeding, it has the potential to facilitate the spread
of HIV as well as other sexually transmitted infections.

REFERENCES:

C. Key facts about LGV
LGV is a sexually transmitted disease spread by certain strains (or serovars) of Chlamydia bacteria called L_1, L_2 and L_3.

Initial infection with these bacteria causes a small, raised lesion within the penis or rectum which is painless. This lesion can turn into an ulcer within three days to one month. Common signs/symptoms associated with LGV include:

- swollen lymph nodes in the groin
- bleeding from the anus

Lab tests specific for LGV are not routinely available, although tests for Chlamydia from samples taken from a lesion or the rectum can help support a diagnosis of LGV.

Treatment for LGV is essential; otherwise, the infection can spread and damage lymph nodes and the intestines, causing scarring. The American Centers for Disease Control and Prevention (CDC) recommends the following antibiotics for treatment:

- doxycycline, 100 mg taken twice daily for 21 days, or alternatively
- erythromycin 500 mg, four times daily for 21 days

Erythromycin has the potential to interact with other medications, including two classes of anti-HIV drugs—protease inhibitors and non-nukes (non-nucleoside reverse transcriptase inhibitors).

Some specialists believe that another antibiotic, azithromycin (Zithromax), taken in a dose of 1 gram once weekly for three consecutive weeks, is effective against LGV. However, the CDC points out that there are no data from controlled clinical trials to support such a conclusion.

REFERENCE:

D. Many questions, no answers
Research into the current outbreaks of LGV in Western countries is necessary, as there are many issues and questions raised by scientists at the CDC and in New York City for which there are currently no clear solutions or answers, including the following:

- Because some symptoms of LGV, such as rectal bleeding, are similar to other conditions such as Crohn’s disease or rectal cancer, it is possible that previous cases of LGV have been missed.
- Simple diagnostic tests for LGV are needed.
- Although LGV appears to be spread through unprotected anal intercourse, the roles of “fisting” and the use of sex toys in transmitting this infection are not clear.
- Strangely, few cases of LGV infection of the penis have been reported. Is it possible that symptom-free cases of LGV infection can exist in the mouth, throat, urethra and cervix?
- Must treatment for LGV continue for 21 days or are shorter regimens also effective?
- Are HIV positive people more susceptible to LGV?
• What role do illicit substances such as crystal methamphetamine play in the transmission or susceptibility to LGV infection?

Answers to these questions are needed to help bring the outbreak of LGV to a halt.

REFERENCE:

II ADDICTIONS

A. Crystal meth: Understanding its allure

Outbreaks of sexually transmitted diseases (STDs)—particularly syphilis, drug-resistant gonorrhea and, more recently, LGV—are occurring against a background of substance use and unprotected sex with many partners among some groups of gay and bisexual men in North America and Western Europe. Exposure to these infections can help facilitate the transmission of HIV, by weakening the immune system and causing sores, ulcers and bleeding in the mouth, penis and rectum. More recently, transmission of at least one case of multi-drug-resistant HIV has been documented in this setting.

If the cycle of dysfunction and multiple infections is to be broken and lives and personal dignity restored, then researchers, policy planners and the staff of public health units and AIDS service organizations desperately need to understand the reasons why some people risk themselves, their health and the lives of their sexual partners. Only when that understanding has reached can rational, humane and effective plans to help stem the HIV/AIDS pandemic be tested and implemented.

Although Treatment Update briefly reviewed the motivations and consequences of exposure to the highly addictive illicit drug crystal methamphetamine, the current issue explores these ideas in much more depth. In our first report, we highlight the many effects of crystal meth on the body and brain. This lays the foundation for our second report, where interviews with crystal meth users reveal why some people with HIV/AIDS or at high risk for HIV/AIDS perceive this drug, at least initially, to be so enticing.

B. Drug twists brain and body

Crystal meth (crystal methamphetamine) goes by several other names, including the following:

• tina
• ice
• meth
• crystal

Because it is part of the amphetamine group of drugs, crystal meth has a stimulating effect and, like all amphetamines, can affect the heart and cardiovascular system, causing the following complications:

• rapid heart beats
• high blood pressure
• short, rapid breaths
• feeling hot

Repeated, regular use of crystal meth (bingeing) can cause inflamed blood vessels and heart damage. All of this can lead to other complications, including strokes and high blood pressure. These complications have been noted in relatively young people not normally at risk for cardiovascular disease but who became at risk due to exposure to crystal meth.

Kidneys and muscles

Crystal meth has also been found to cause muscle breakdown, leading to kidney damage. In one study of people who sought help from the Emergency departments of California hospitals, researchers found that 43% of patients with muscle breakdown and kidney damage had crystal meth in their urine samples.

Infection and immunity

In laboratory experiments, crystal meth appears to weaken a key group of cells of the immune system, CD8+ cells. They are responsible for fighting infections, including HIV.

In one study, long-term use of crystal meth was associated with an increase in gum disease. The stimulation and agitation caused by crystal meth was likely responsible for participants in that study having partially worn down their teeth by clenching and grinding their jaws.

No regulation

Because regulatory agencies do not monitor or assess the production, purity and safety of crystal meth, it is not surprising that batches of this drug can be contaminated with other compounds. The
production of crystal meth is a toxic affair and lead poisoning has been reported in some users.

**Juggling drugs**

Crystal meth and chemically related compounds such as ecstasy are broken down by enzymes in the intestine and liver. Two classes of anti-HIV medications are also processed by these same enzymes:

- protease inhibitors (PIs)
- non-nukes (non-nucleoside reverse transcriptase inhibitors)

When two different compounds are processed simultaneously through the same enzyme, levels of one or both drugs can either rise or fall, leading to increased side effects or drug resistance. In the case of crystal meth, PIs and non-nukes have the potential to increase levels of this drug to very high levels. At least one person has died because of this interaction.

**Crystal on the brain**

Perhaps the most disturbing and obvious impact of long-term exposure to crystal meth is its many effects on the brain. Experiments on rats suggest that the concentration of crystal meth in the brain is about 10 times greater than that found in the blood after the animals have been given the drug. In people, crystal meth appears to last a relatively long time, with 50% of the drug being detectable 12 hours after a dose was taken. These findings suggest that meth concentrates in the brain and likely lasts a relatively long time in this organ. Thus the brain may bear the brunt of crystal meth's toxic effects.

Cells in the brain use compounds called neurotransmitters, including serotonin and dopamine, to send signals to each other. These compounds also play a role in many functions, including memory, mood, muscle control and learning.

In one study of 15 HIV negative, long-term crystal meth users, researchers scanned their brains with hi-tech PET scanners. The scans revealed less-than-normal levels of molecules used to move the neurotransmitter dopamine to cells. This likely reduced the ability of brain cells to get access to dopamine and possibly affected their ability to store and retrieve information as well as control muscles. Not surprisingly, further research found that the participants had difficulty learning and coordinating the movement of their muscles.

**HIV and crystal meth**

Based on the results of test-tube and animal experiments, some researchers suggest that crystal meth has the potential to make HIV-related brain damage worse. Possibly, the mixture of crystal meth and toxic proteins produced by HIV could increase the risk of AIDS-related problems involving clear thinking and memory. But long-term studies of HIV positive crystal meth users are needed to confirm this theory.

**Crystal enters the body**

There are many ways in which this substance can enter the body. Crystal meth can be:

- snorted
- swallowed
- injected into blood vessels
- squirted into the rectum

Depending on which method is chosen, the high from crystal meth can occur anywhere from one to 20 minutes after the drug is taken. Initially, users have reported the following feelings:

- a heightened sense of alertness
- euphoria
- an increased sense of well-being and confidence

But doctors have also observed other, less glamorous effects of crystal meth in users, such as:

- personality changes
- restlessness
- tension
- irritability
- problems falling asleep
- loss of appetite
- unintentional weight loss
- verbally threatening and sometimes physically aggressive behaviour

Because 50% of crystal meth leaves the body within 12 hours of being taken, its pleasurable effects can wane within this time frame. Users often take another hit of the drug to avoid the following symptoms of withdrawal:

- depression
- lack of energy
- loss of pleasure from everyday activities
- thoughts of suicide
The downward spiral
Continued use of crystal meth over several days can lead to an “extremely irritable and paranoid state,” according to researchers. What’s more, in about 10% of long-term users, exposure to this drug can lead to a state of psychosis with the following features:

- feelings of paranoia
- disconnection from reality
- intense hallucinations

Recovery
Crystal meth users who enter treatment programs appear to recover from some effects of this drug. For instance, in a study of 170 crystal meth users, 23% reported feelings of paranoia when they entered a treatment program. Between two and five years after completing the program, only 7% still had feelings of paranoia.

 Sadly, 62% of 170 participants were depressed when they entered the program and the same proportion remained depressed when they left. And 28% of participants reported violent behaviour in the year after they had left the program, according to the research team. Overall, these findings suggest that crystal meth exposure can cause lasting damage in some people.

Crystal meth impairs the brain’s ability to make and possibly use the neurotransmitter dopamine, and HIV appears to damage dopamine-producing parts of the brain. Some doctors who treat people with HIV/AIDS (PHAs) recovering from meth addiction have found the antidepressant bupropion (Wellbutrin, Zyban) useful for managing depression in their patients. Because antidepressants take weeks or even months to begin to work, these drugs are not suitable for treating withdrawal from substance use. Many other compounds are being tested for their anti-addiction effects in crystal meth users, including anti-schizophrenia medicines. And, of course, medication(s) are used together with different forms of counseling, 12-step programs and harm reduction messages to help people begin the process of healing and recovering their lives from substance use.

REFERENCES:

C. Sex, lies and crystal
To better understand what motivates people to use crystal meth, Dr. Steven Kurtz at the University of Delaware’s Center for Drug and Alcohol Studies conducted several small focus groups with gay and bisexual men who used this drug. Some of the men involved in the study were HIV positive. Although the number of participants was relatively small (15 men) the findings begin to reveal the state of mind that predisposes some people to use crystal meth. Moreover, the findings could be used to design other studies with more diverse populations in other cities so that researchers can better understand what places some people at risk for crystal meth exposure and addiction.

Study details
In 2003, Dr. Kurtz recruited and interviewed 15 men between the ages of 33 and 50. Eight men were Hispanic and seven were white. Seven of the men were using crystal meth during the period when the research was conducted. The remaining eight men described themselves as recovering from addiction to this substance. Six of the seven current users said that they were HIV negative, while six of the eight former users said that they were HIV positive.

Why use crystal meth?
Dr. Kurtz found that there were three general patterns that underlay participants’ perceived vulnerability to substance use. For some people, crystal meth appeared to initially help them do the following:

- escape loneliness
- deal with feelings of sexual unattractiveness
- lower sexual inhibitions

What is perhaps disturbing is that, as a result of the interviews, Dr. Kurtz says that “these problems appeared to stem from deep-seated feelings of being unloved and unlovable.”
All of the focus group members agreed that substance use among men who have sex with men (MSM) was a way of coping with “the social difficulties that they faced living in a homophobic culture.” Substance use helped these men avoid the realities of being “alone, unacceptable and unloved.”

**Aging and illness: releasing the inner chemist**

According to Dr. Kurtz, middle-class American gay male culture “values sexual attractiveness and prowess to a degree that is unreachable for many men.” Therefore, some MSM who are aging, ill or both worry about their attractiveness. One doctor who was part of the focus group said the following:

“I see guys when they get into their late thirties and early forties, that’s when they get into real trouble: ‘I’m in my late thirties, early forties; I’ve got to get everything I can get now before my hair falls out.’ And they just get annihilated. See, guys in their twenties, they call it partying. They take ecstasy before they go to a dance club. These guys in their late thirties are the ones that are doing the ‘I need a little bit of this, a little bit of that,’ and they think they’re chemists. They do one little thing, too much of something that doesn’t balance out something else, and they’re in trouble.”

**Sex and crystal meth**

All of the participants had used crystal meth while having sex and all but four of them did so in group settings. One former user noted that there are reasons for this:

“Being high on crystal in sexual situations, you need excessive amounts of input, of stimulation, just to keep that end of the buzz going... The most important thing for you is that you are doing it with other people who are of the same mindset, but also at the same level of buzz. It does not matter who you are having sex with, near or whatever, as long as they are just as high as you and on the same thing. That becomes your overriding concern.”

**The dark side of crystal**

Participants who were recovering from crystal meth addiction were previously able to use the drug on a regular basis for as little as a few months to as much as 10 years before serious problems developed. What is interesting from their personal accounts, according to Dr. Kurtz, is that “events that led the men to begin using the drug were similar to ones that led them to stop—events that revolved around personal relationships and sex.”

Perhaps a common thread that linked many participants’ initiation of crystal meth was “making connections.” Yet for many men, regular use of crystal meth “became a barrier rather than an aid to friendships,” according to their interviews. According to one interviewee who found that using crystal meth became a substitute for dating:

“It gets to the point where you feel like people are against you. Well, let me say that I’ve messed up my relationships because I’ve chosen to be on crystal meth, and then I start thinking to myself, ‘You know what, I really don’t need a relationship.’ Where before the initial high I was thinking, ‘Oh yeah, I’m going to have a relationship with this guy, so let me go meet him.’ I’ve lost many relationships because of my stupid high.”

Initially, the sexual adventures and stamina that were part of crystal meth’s allure began to cause problems for many users who had long-term relationships.

Not only did several men lose their romantic relationships because of crystal meth, they also lost their jobs and businesses because it caused the following problems:

- interfered with reporting to work on time
- interfered with their judgment while at work
- caused them to lose the trust of coworkers

Many users developed paranoia, which, according to Dr. Kurtz, “led to increasing isolation from the sex scenes that participants initially claimed to have found so enlightening and liberating.”

**Crystal’s wear and tear**

Some men may have initially felt better about their appearance when using crystal meth. But long-term use of this substance began to take its toll on users, many of whom began to disappear from public life, as one participant noted:

“People who get sucked into crystal use very, very quickly drop out of sight. You don’t see what happens to them. You don’t see that they plucked all the hair out of their eyebrows. You don’t see the sores on their skin. You don’t see the sunken-in cheeks. You don’t see their pupils bigger than their whole head. You don’t see that really ugly thing, the ugly, physically ugly
Initially, crystal meth seemed to help the men have uninhibited sex, but Dr. Kurtz also found that its use “led many men to take sexual risks that they would not have if they had not been high on the drug.” For some participants, the discovery that they had health problems, such as infections with STDs, including HIV, was a sign that their use of crystal meth was out of control.

Shattered dreams
In addition to the risk of HIV and other STDs, many users found that repeated exposure to crystal meth became “less fulfilling with time.”

Perhaps a clearer understanding of the type of connection that crystal meth really fosters is revealed by one man who still uses the drug:

“When I first signed up on one of the ‘party and play’ websites, I posted a picture of my face on my profile. I wasn’t getting so many hits. When I posted a picture of my dick instead, then I became really popular right away.”

The fantasy becomes reality
Because exposure to crystal meth causes people to have difficulty distinguishing between reality and fantasy, quitting isn’t easy, according to one former user:

“A lot of people don’t realize exactly how quickly crystal becomes addictive. The thing that makes crystal so insidious is that even if you were basically a mentally healthy, well-adjusted, happy person beforehand, the first couple of times after you do crystal it manages to convince you that the state you are in when you are high on crystal is the normal, desirable, natural state, and that what happens to you when you are off crystal is the abnormal condition that needs to be rectified... I don’t think that a lot of people are prepared for how fundamentally it changes the way you think on and off the drug.”

Repairing the damage
Although this study was small, its findings provide some insight into why crystal meth becomes so alluring. It also highlights the many dangers of the drug. Perhaps what is most useful about this study is that it is a snapshot of some aspects of middle-class gay male culture that is generally not glamourized in gay media. Dr. Kurtz states that the participants in his study revealed that “many gay men feel isolated, often use drugs in an attempt to bond with others, and find that connectedness and intimacy remain elusive.”

Programs that aim to reduce the harm from crystal meth exposure and sexual risk-taking may be more effective, he says, if they can address “the men’s needs for—and skills at attaining—social connectedness to other individuals.”

Dr. Kurtz has presented some ideas that need to be tested. Hopefully, other researchers will confirm and extend his findings so that successful interventions to reduce the harm posed by crystal meth can be developed.

REFERENCE:
What CATIE Does

The Canadian AIDS Treatment Information Exchange (CATIE) is committed to improving the health and quality of life of all people living with HIV/AIDS in Canada. CATIE serves people living with HIV/AIDS, and the people and organizations that support them, by providing accessible, accurate, unbiased and timely treatment information. CATIE provides such information through a comprehensive Web site, a bilingual toll-free phone service, electronic and print publications, a national reference library and workshops and exhibits at conferences across Canada.

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