The Anal Dialogues

Rectal microbicides-topical gels, ointments and lubricants laced with drugs to block HIV-could help stop the spread of the virus. So why is it taking so long to develop them? For one thing, an unwillingness to talk about sex-especially anal sex. Given the potential of microbicides' protective power, it's time we loosen our tongues in order to start saving lives.

July 1, 2011 By Trent Straube

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In 1992, at a meeting of the Delaware Valley Women and AIDS Network, Anna Forbes first heard about experimental compounds called vaginal microbicides. It sparked an "A-ha!" moment for the longtime advocate for women's health. Forbes saw right away how a microbicide—a gel, cream, lubricant or other topical agent that could be applied to the vagina to inhibit sexual transmission of HIV—would offer a much-needed method of protection to women, especially those who couldn't get their partners to use condoms. And as an advocate for gay men's health, Forbes also imagined how a rectal microbicide could offer a valuable prevention tool for anal sex for both men and women.

Women and gay men share the common concern of having their health needs respected and addressed, Forbes says. "A receptive partner is a receptive partner." Effective microbicides would arm both male and female receptive partners with prevention tools that could save their lives.

But when she started talking about the notion of vaginal and rectal microbicides, Forbes found that even people on the cutting edge of women's and gay men's health advocacy were uncomfortable talking so specifically about sex, especially anal sex. It showed, according to Forbes, "this weird way that homophobia and sexism intersected." And it pointed out "the well-kept secret that women have anal sex too."

Undaunted by the reluctance of many of her peers, and inspired by the potential lifesaving power of microbicides, Forbes set out to convince the world to think similarly, working for a decade at the Global Campaign for Microbicides (she recently moved into consulting). The topic continued to be a hard sell. "The trouble with microbicides in comparison to pills and injections," Forbes says, "is that they are applied 'down there.' You can't talk about microbicides without talking about sex."

Thanks in part to the unflagging efforts of Forbes and other visionary leaders (along with increasingly promising research data), the scientific and advocacy communities began rallying

around vaginal microbicide research. Yet, very few people supported the notion of a rectal version. Forbes recalls the first time she saw the topic discussed in the print media, in a 1999 *POZ* article, "Beyond Condoms: Life After Latex," in which journalist Michael Scarce presciently wrote: "The astonishing thing is, gay men raise no voice to advocate for a form of HIV prevention that maximizes pleasure and safety." In Colorado the next year, at the second LGBTI Health Summit (the initials embrace lesbian, gay, bisexual, trans and intersex people), Forbes gave a presentation on the need for rectal microbicides. Only about five people showed up. Clearly, interest in the subject was lacking—even among the most likely benefactors, gay men.

Then, another A-ha! moment: The messenger, Forbes realized, needed to double as the message. A straight woman couldn't draw the same attention in the gay community as a gay man could. "We needed a gay male face, somebody with a track record in the [prevention] field," she says. She envisioned an organized group led by a gay man working to promote rectal microbicides and in the process tackling the taboos associated with anal sex. In 2005, Forbes approached some likely advocates: Marc-André LeBlanc from the Canadian AIDS Society, Julie Davids from CHAMP (Community HIV/AIDS Mobilization Project) and Jim Pickett of the AIDS Foundation of Chicago. Although all were overextended, they agreed on the need to fight for a new form of prevention. Thus, the International Rectal Microbicide Advocates (IRMA) group was formed.

IRMA began modestly. "We had a listserv, and our goal was to get people to share information [about rectal microbicides]," says Pickett, IRMA's chair (its out, gay face). He recalls begging people at the 2005 National HIV Prevention Conference to join the email group. Many resisted, arguing that rectal microbicides were too futuristic and that advocating for them would deflect resources from the priority concern at the moment: condoms. "People would almost groan when Jim would get on stage," says Ian McGowan, MD, a leading microbicide researcher.

People's reluctance to talk about butts (male and female), similarly muzzled scientists. As recently as a few years ago, many researchers scoffed at the very idea of a rectal microbicide, claiming human anatomy made it impossible. Unlike the vagina, which is essentially an enclosed container, the five-foot-long colon, Pickett says, is "like the Holland Tunnel." There was the question of how far ejaculate could travel up the colon. Would the colon's entire surface have to be protected? How much gel would be required—and how much could a body take? Scientists didn't know. That is, until Craig Hendrix, MD, at Johns Hopkins University, conducted experiments involving some brave volunteers, faux microbicides and a hollow dildo that squirted an "ejaculate" traceable by MRI scans. (Read one volunteer's hilarious account, "Putting My Ass on the Line," on the IRMA blog at irma-rectalmicrobicides.blogspot.com.) The experiments proved that the faux microbicide traveled well with the ejaculate and that to be effective, a microbicide would likely need to coat only the lowest 4 to 6 inches of the rectum and anal canal. Furthermore, researchers determined that humans could tolerate up to 30 milliliters (ml) of gel administered anally. However, the gel currently being studied requires only 4 ml, less than a teaspoon.

If these details make you squirm, you wouldn't want Pickett's job. The gregarious advocate constantly finds himself discussing anal sex and all its details—often in front of crowds. He does so as easily as most guys rattle off sports stats, employing honesty and humor that prove disarming.

Equally important, he and IRMA back up their cause with something scientists recognize: cold, hard data.

Perhaps IRMA's most visible work is three game-changing reports it published in conjunction with the biennial International Microbicides Conference. The first, *Rectal Microbicides: Investments & Advocacy* in 2006, compiled what research was being done and where—a tricky task. "A lot of researchers were concerned that if 'anal' or 'rectal' appeared in research proposals or reports, they wouldn't get funded, so they'd scrub their papers so those words wouldn't show up," LeBlanc says. "Instead, they would refer to 'topical use of products' or other language." And because of the dangers surrounding the subject—male-to-male sex is illegal in many countries, including 31 in sub-Saharan Africa—IRMA first had to gain researchers' trust, proving they were not raging advocates who would alienate and antagonize. Their professionalism paid off, and the report was a hit. "It showed we were serious," Pickett says, "and we got hundreds of new members."

The next two reports, *Less Silence, More Science* in 2008 and *From Promise to Product: Advancing Rectal Microbicide Research and Advocacy* in 2010 (all the reports are available at rectalmicrobicides.org), addressed the reality that anal sex is more common than believed. The reports showed that among women anal sex remains an overlooked driver of the AIDS epidemic. (Because there are more women in the world than gay men, the overall number of women having receptive anal sex is higher than that of gay men.) By amassing data and research from across the globe, the reports argue effectively for developing rectal microbicides. A sampling from the 2010 report:

- It is estimated that unprotected anal intercourse transmits HIV 10 to 20 times more effectively than unprotected vaginal intercourse.

- Gay men in the developing world are 19 times more likely to be positive compared with the general population.

- In the United States, men who have sex with men (MSM) represent 53 percent of new HIV infections.

- Depending on the study, 20 to 75 percent of women report having engaged in receptive anal sex.

- Globally, up to seven times more women than men have receptive anal sex.

To confront homophobia and varying cultural and religious belief systems that complicate HIV prevention (for example, the tendency in Africa to focus solely on vaginal transmission), IRMA launched Project ARM (Africa for Rectal Microbicides) and IRMA-ALC (IRMA-America Latina y el Caribe).

Beyond advocacy and education about anal sex, IRMA helps shape a unified research agenda, coordinating studies among disparate, often unconnected researchers across the globe. ("We herd the cats," Pickett says.) It directs funds to needed areas (though it doesn't directly fund research). It digests complex research into talking points for mainstream media, translates reports into other languages, asks important questions and pursues answers.

Along the way, microbicide research has produced some immediate benefits. At a 2006 Cape Town AIDS conference, biomedical scientists with the Population Council presented data on the possible link between anal lubes and HIV risk. (The same team, lead by David Phillips, PhD, reported in 2000 that the spermicide nonoxynol-9 damaged linings of the rectum and vagina, thus increasing the risk for HIV and herpes—findings that resulted in N-9 being removed from most condoms.) The lube presentation, Pickett says, sparked his own revelatory moment. "We were like, The lubes we have are not tested for safety? We have to get research on this. Yes, we want rectal microbicides, but people are using lubes today!"

At the time, little was known about the popularity, use and safety of anal lubes—in the United States, lubes must be tested for vaginal irritation (in rabbits) but not for rectal use. To build a research database, IRMA conducted a survey. "We thought we'd get a few dozen answers," LeBlanc says, "but we had nearly 9,000 people respond from nearly 100 countries." The survey was translated into six languages. "As far as we know, it's the largest survey on anal sex in the world." (IRMA is following up with a survey on douches and enemas, which might affect HIV/STI risk and offer a mode of microbicide delivery.)

The survey results have been pivotal to researchers such as Charlene Dezzutti, PhD, a lab director at the Microbicide Trials Network, who is examining the lube qualities that might affect HIV risk and be of use in microbicides.

IRMA's hard work is paying off elsewhere too. The energetic listserv now includes more than 1,000 members. Pickett manages its daily conversation from his office at the AIDS Foundation of Chicago (AFC), where he is director of advocacy (IRMA is a project of AFC). "I think the overarching thing that has made us successful is that we bring together scientists and advocates," Pickett says. "There is no other forum like this. An advocate in Thailand can post an opinion, and a researcher in Peru or London or Pittsburgh can comment all in the same hour—people find it really useful."

Discussions range across prevention topics including study results, female condoms and Uganda's Anti-Homosexuality Bill. One round of emails discussed a British safe-sex musical video with the problematic lyrics, "Something to remember as a rule of thumb, one up the bum and there's no harm done…one up the bum and you won't be a mum." (Listserv members contacted the video's creators to argue against promoting anal intercourse as a risk-free way to avoid getting pregnant.)

“[IRMA is] doing all the right stuff,” says Forbes, speaking like a proud momma. “They’re recognizing the importance of geographic and constituency diversities, and they’re promoting everybody having the discussion in whatever way makes sense in their own communities and encouraging people to share ownership—exactly what we need.”

This year, IRMA had good news to trumpet. A Microbicide Trials Network study, MTN-006, found that people who used a rectal gel containing 1 percent tenofovir, an HIV drug, had high concentrations of the med in rectal tissue and lower concentrations in the blood stream, which could mean fewer side effects. The downside: A single dose before sex probably won’t be effective.

Today, people no longer groan when Pickett takes the stage. “People came up to me after the CAPRISA results [a large South African microbicide study] and said, ‘For all these years, I thought you were crazy, but you’ve proven me wrong. Now I understand why you had such a belief in this.’”

Perhaps IRMA’s biggest success is simply getting people to confront the realities of anal sex and HIV. Because without honest dialogue about sex—whether at an international science conference, a sex education class or an intimate chat between lovers—we are never going to stop this epidemic. And that’s something we all need to speak up for.

Slippery Slopes
Can lubes increase the risk of HIV during anal sex?

A slew of recent studies suggest that using lubes for unprotected anal sex may increase the risk of HIV, and that some lubes may harm the rectum’s thin protective layer of cells (the epithelium). It’s premature to know which brands to avoid, says Marc-André LeBlanc, a lube advocate with the International Rectal Microbicide Advocates (IRMA). Most research has been done in laboratories, and it isn’t certain whether the findings translate to humans—or whether the products’ lubricating benefits outweigh their potential harm. But one fact is certain: “The best way to prevent acquiring HIV and STIs [sexually transmitted infections] during anal sex is still using male or female condoms,” LeBlanc says. “And we know that using lubes with condoms decreases the risk of the condom slipping or breaking—a big bonus.”

In the meantime, here’s a highlight of what scientists are investigating and how lube qualities might affect the success of microbicides:

- Polyquaterniums, a class of chemicals common in cosmetics, seem to increase HIV replication by almost four times in lab tests. A Population Council study found this ingredient in three of four HIV-enhancing Astroglide brand lubes: Astroglide Liquid, Astroglide Warming Liquid, Astroglide Glycerin & Paraben Free liquid and Astroglide Silken Secret.

- Osmolality refers to the concentration of salts, sugars and other substances (solutes) present in a lube. Hypo-osmolar lubes have a lower concentration of solutes than human cells and cause the cells to swell with water and burst. Hyperosmolar lubes cause cells to shrink and become brittle. Iso-osmolar lubes don't affect cells because their concentrations are identical. Most water-based lubes are hyperosmolar and damaging.

- pH balance is acidic in the vagina and neutral in the rectum. Many lubes are designed for the vagina—does the difference in pH mean they affect the rectum differently?

- Good and bad bacteria live in a delicate balance in the vagina and gut. Will disrupting this balance make the rectum more susceptible to HIV?

- Viscosity is the slippery quality that gives lube its feel and texture. Glycerin, in water-based lubes, adds to viscosity. It also makes lubes hyperosmolar—and destructive to epithelium. When a rectal microbicide now in trials proved harmful to the epithelium, researchers solved the problem by lowering the glycerin content.

Charlene Dezzutti, PhD, with the Microbicide Trials Network and the University of Pittsburgh, looked at these qualities in six popular lubes. Some findings: Pré and Wet Platinum appear safest. Pré is the only water-based lube that is iso-osmolar and doesn't damage the epithelium. KY Jelly wiped out entire colonies of good bacteria. Astroglide is the most hyperosmolar and most toxic to cells and tissue (Elbow Grease, ID Glide and KY Jelly have similar toxicity profiles). But Dezzutti also warns that more studies are needed before any official warning or suggestions can be issued.

Starting to Gel
Microbicides: Where they are now and where they are going

VAGINAL GEL: After two decades of disappointing results, a breakthrough arrived last summer with results of the CAPRISA 004 trial: Women using a gel containing 1 percent tenofovir (an HIV med found in Atripla, Viread and Truvada) had 39 percent fewer infections than those using a placebo. Women with 80 percent adherence to the two necessary applications per sex act (12 hours before, then immediately after) had even fewer infections. The gel also offered protection against herpes.

What's Next: Studies are under-way to confirm CAPRISA 004 results and determine the most effective concentrations and doses, but the global economic crisis has depleted funding, slowing progress. On the bright side, the drug from the vaginal gel is showing up in rectal tissue, so one product might offer women protection in both areas.

RECTAL GEL: Microbicide Trials Network study MTN-006 looked at using the vaginal tenofovir gel rectally, with promising results announced in February. Although the vaginal formulation harmed the rectal lining and caused gastrointestinal distress, Charlene Dezzutti's team developed a better version with less glycerin. And, says Ian McGowan, PhD, a co-principal study investigator, "We found that when you give the drug topically, you get very high concentrations in the rectal tissue—a hundred times the amount from a single Viread tablet." A few caveats: Tenofovir works not by directly attacking and disarming HIV, but by accumulating in the tissue and CD4 cells HIV will attack, preventing HIV from replicating once it invades the cell. Unfortunately, this accumulation demands repeated doses. "I think MTN-006 suggests," McGowan says, "that if you just take one dose, orally or rectally, half an hour before exposure, I would doubt you'd be protected."

What's Next: A Phase I study (MTN-007) on the safety and acceptability of the rectal tenofovir gel; and Project Gel, investigating the use of rectal microbicides among African-American and Latino men who have sex with men (MSM). "It's critical," McGowan says, "because these are the people who are getting infected and need the product."

FUTURE IDEAS AND EXPERIMENTS:
Other HIV meds or combos—or completely new compounds—may offer better protection than tenofovir as microbicides (hint: HIV drugs that are too toxic as pills may work as topical solutions).

Different modes of delivery: How about a slowly dissolving ring instead of a vaginal gel? Or combining a microbicide with a vaccine, to help prepare the immune system for an encounter with HIV? And vaginal probiotics—living microbicides—could be created by genetically altering bacterial cultures such as the common lactobacilli.

Research is showing that HIV might lower the electrical barrier of epithelial cells, enabling infection even without surface damage. Such new knowledge could produce future strategies and modes of protection.

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http://beta.docker.poz.com/article/Microbicides-Anal-HIV-20673-6286