A Gut Feeling

Having HIV may mean dealing with gastrointestinal problems, whether from the effects of the virus or side effects from antiretrovirals. But these days you shouldn't have to simply put up with problems such as diarrhea, gas, heartburn, nausea, vomiting or constipation.

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Atripla (efavirenz/enofovir/emtricitabine), the single-tablet antiretroviral regimen that ushered in a new era of simplified HIV treatment, introduced Scott Brynildsen to a period of gastrointestinal misery.

HIV positive since 1996, the 37-year-old Seattle resident went on Atripla in 2009. The treatment failed to fully suppress Brynildsen's virus while succeeding in greatly diminishing his capacity to have a bowel movement.

"Trying to pass a stool was agony, and very time-consuming," Brynildsen (pronounced "Burr-NELL-son") says of his struggle with constipation. Speaking with a trademark dry wit, he continues, "It would always come out in one large, angry stool, with animosity, regret, remorse, everything. I watched part of my childhood go by."

Hoping to find a more successful, less side-effect-laden regimen, Brynildsen's doctor switched him to Norvir (ritonavir)–boosted Truvada (tenofovir/emtricitabine) and Reyataz (atazanavir). And while his virus did go undetectable, for the following four years, Brynildsen suffered through the indignities of bloating and gas, which led to considerable physical discomfort and made him feel overweight and unattractive.

"Obviously, I was not a happy person," he recalls.

HIV literally strikes at the gut level. An estimated 55 to 60 percent of the body's CD4 cells are located in the lining of the gut, including the small and large intestines and colon.

Research in both primates and humans has found that HIV launches a major assault on these immune cells as soon as a week after infection, causing serious damage that progresses over the subsequent months. While antiretrovirals (ARVs) appear able to restore these cells to a certain extent, a significant portion of the damage is typically permanent.

W. David Hardy, MD, a clinical professor of medicine at the University of California, Los Angeles, suggests thinking of the gut as essentially outside of the body. A long tube that starts at your

mouth and throat and ends at your rectum and anus, this passageway is designed to process and absorb the good stuff, like vitamins and nutrients, while warding off unwanted pathogens, such as funguses, parasites, bacteria and viruses.

CD4 cells in the gut serve as a kind of immunological shield. When this line of defense is compromised, the toxic invaders can lead to inflammation and wreak other havoc in the gut. Consequently, people with HIV may be more likely to suffer from diarrhea, acid reflux and heartburn, gas and bloating, and nausea and vomiting.

Complicating matters, many ARVs lead to gastrointestinal (GI) side effects, as Brynildsen learned. He eventually switched to Complera (rilpivirine/ tenofovir/emtricitabine), and presto, he was finally free of side effects, able to patch up his tortured relationship with his digestive tract. Until recently, that is. A few months back he began developing diarrhea, which he thinks is likely a result of an adjustment in medication he takes for restless leg syndrome.

Diarrhea is particularly prevalent in the HIV-positive population, with at least one in five people on ARVs complaining of the symptom, according to recent surveys as well as the results of the clinical trials of HIV medications.

However, Rodger MacArthur, MD, director and principal investigator at the Newland Immunology Center of Excellence in Southfield, Michigan, says this may be a low estimate, because it overlooks more minor cases that people with HIV may not think to mention. Diarrhea is graded on a four-point scale, from mild to severe. Most clinical trials only ask about grades 2 through 4—excluding a significant proportion of people with grade 1 who may be greatly troubled by this side effect and how it affects their everyday lives.

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MacArthur argues that diarrhea among people living with HIV may also be under-recognized because, as patient surveys have suggested, physicians don't typically ask about the problem. "Perhaps they think the patients themselves are going to bring it up," he says.

It's important to appreciate that mentioning any side effect to your health care team is vital for your overall health and well-being, in no small part because associating your meds with something negative may make you less likely to stick with your drug regimen. Poor adherence can give HIV the chance to thrive and can lead to drug resistance and treatment failure. The bottom line is you should talk with your clinician about any side effects you're experiencing, as well as any remedies you're using or are thinking about trying.

One way to cope with GI troubles brought on by meds is to switch to a new regimen. (Although keep in mind that many such side effects may occur for just the first few weeks or months you spend on a new regimen, so you may be able to wait them out.)

"I don't see any reason why people should have to live a life of discomfort or side effects if there are alternatives," says Joel Gallant, MD, MPH, medical director of specialty services at Southwest CARE Center in Santa Fe, New Mexico.

“Obviously when you switch you have to be aware of the potential of resistance and things like that. But especially if someone is on their first regimen and doesn’t have resistance, we can switch them to just about anything and they’re going to continue to do well. And most people, if things do get better, are really grateful that they switched,” he says.

While many ARVs may cause diarrhea, the major culprits are protease inhibitors as well as two “booster” drugs, which raise blood levels of other HIV meds: Norvir (ritonavir), which is included in Kaletra (lopinavir/ritonavir); and Tybost (cobicistat), which is a component of Prezcobix (darunavir/cobicistat), Evotaz (atazanavir/cobicistat) and Stribild (elvitegravir/cobicistat/tenofovir/emtricitabine).

While over-the-counter diarrhea medications might seem like a logical remedy, MacArthur cautions against “antimotility agents” such as Imodium (loperamide). These drugs draw water out of the gut and essentially shut it down, putting you at very high risk of constipation, or the more severe form of the condition, obstipation. Additionally, they have never been studied for safety and efficacy among people with HIV.

At the end of 2012, the first medication specifically approved to treat HIV medication-related diarrhea, called Mytesi (crofelemer)(formerly known as Fulyzaq) , hit the market. In the study that led to the approval, 374 participants with a median 2.5 watery bowel movements a day took the drug or a placebo. A total of 17.6 percent of those taking Mytesi got down to two or fewer watery bowel movements a day, compared with 8 percent on the placebo.

Gallant says a potential answer for both diarrhea and constipation is in the use of fiber supplements, such as Metamucil, which can absorb some of the excess water in the event of the former problem and add helpful bulk for the latter. (Caution: Make sure to properly dilute the fiber in plenty of water and stir well, and drink it immediately, before it develops into a more solid mass that puts you at risk of choking.)

There is also a chance that an infection is the cause of the diarrhea. Your clinician will want to run tests and then may prescribe antibiotics or antiparasitic medications.

Dietary shifts may also help alleviate diarrhea. While spicy foods often exacerbate the problem, everyone’s body is likely to have its own idiosyncratic response to whatever gets tossed down the hatch. So you are probably your own best judge on what to avoid. However, note that people become temporarily lactose intolerant when they have diarrhea, so avoid milk products.

Brynildsen laments that romantic engagements are difficult for him because of his bad reactions to certain foods, dairy products in particular (he professes a fondness for cheese). “‘I’d love to go out and have a nice fine dining experience with you,’” he says to an imaginary date, “‘except that looks like Alfredo sauce and it’s going to ruin our night.’”

Another potential HIV treatment-related side effect is nausea, although it is rarer these days, and if it occurs tends to be only in the short-term.

“What I tell people is, unless you’re instructed differently, almost always take your medications with food,” Hardy advises. “Food seems to have a buffering effect that decreases either the contact time or the mixture of stuff that actually touches the gut wall.”

One exception to the take-with-food guideline is if you’re on Sustiva (efavirenz), which is included in Atripla and needs to be taken on an empty stomach to be absorbed properly.

As for nausea, in the early days of HIV treatment, when options were limited, clinicians might have prescribed an anti-nausea medication to help you fight queasy reactions to meds. Today switching ARVs is the much more likely answer. Otherwise, age-old remedies like carbonated beverages or ginger, including ginger ale or ginger candy, can be effective.

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Gas and bloating is yet another potential ARV side effect. Gallant says that physicians are more inclined to simply discuss with their patients how best to deal with gas and bloating, rather than switching medications. One option is to try an anti-gas drug such as Gas-X (simethicone). If someone is greatly bothered by gas and bloating, Gallant says he sometimes will consider suggesting an HIV regimen switch.

Lastly comes the subject of acid reflux and heartburn. The big problem here is that drugs used to treat the condition shouldn’t be combined with many of the ARVs.

There are three main kinds of treatments for acid reflux and heartburn, all of them available over the counter: antacids, such as Tums tablets or liquid Mylanta, which operate quickly and provide more short-term relief; H2 blockers, such as Zantac (ranitidine), which take more time to work but also work longer; and proton pump inhibitors (PPIs), including Nexium (esomeprazole) and Prilosec (omeprazole), which are taken daily for continuous treatment.

Conflicts arise with HIV meds Edurant (rilpivirine), which is a component of Complera, as well as Reyataz (atazanavir), which is included in Evotaz: Both of these drugs need an acid environment to be properly absorbed. People taking either of them are advised to be very careful with taking antacids, in particular the longer-acting H2 blockers and proton pump inhibitors; Gallant says it’s usually safer just to switch HIV meds.

In addition, all of the integrase inhibitors are sensitive to calcium, magnesium, iron and aluminum, which are often found in dietary supplements, laxatives and most antacids. Anyone on Isentress (raltegravir), Tivicay (dolutegravir), Vitekta (elvitegravir), Stribild or Triumeq (dolutegravir/abacavir/lamivudine) should avoid antacids two hours before or after taking their ARVs. It is all right to take integrase inhibitors with H2 blockers or PPIs.

Lifestyle shifts to consider when coping with acid reflux and heartburn include eating more frequent, small meals rather than a few large ones, and avoiding eating before bed. You can also try elevating the head of your bed about 30 degrees. You need your entire upper body at an angle, not just your neck; the idea is to keep acid from drifting up into your esophagus. So you’ll have to

prop up the legs at the upper end of the bed, or use a large wedge on your mattress that's designed for acid reflux relief.

For dietary shifts, the rules are similar to those for diarrhea: Trust your intuition, and try to get a sense of which foods are more likely to cause you problems—perhaps spicy things—and avoid them whenever possible.

As for Brynildsen's recent resurgence of GI-related woes, he's determined to find answers. After all, he's about to go back to school and can't let extended bathroom breaks interrupt classroom time.

"You don't have to live in fear of embarrassment," he says. "I find that eating healthier and maintaining a very strict medications schedule are highly beneficial. It makes it easier to do the things I want to do."

His recent bout with diarrhea aside, he still says that switching from his triple-pill cocktail to Complera has been "a dream come true" for him.

"If I want to go on a long road trip," he says, "I can actually do that now."

Click here to read tips on managing gastrointestinal problems.

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