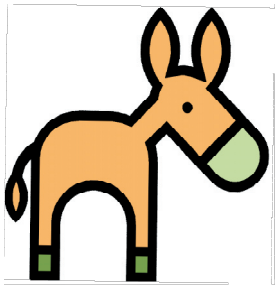
The Pitt Men's Study

news and notes *Spring 2010*

Pitt Men's Study Begins Anal Cancer Screening



Here at the Pitt Men's Study we are as interested as ever in your anus! In fact at your next visit we may be asking you to have an anal Pap smear. The test is similar to a cervical Pap smear. A health professional will use a swab like a Q-tip to collect cells from the anal canal. Then a lab analyzes the collected cells under a microscope. It is a painless procedure.

So why are we so bent on exploring your anus? Well, it is now well established that gay and bisexual men, in particular HIV-positive men who have sex with men, are at greatly increased risk of developing anal cancer when compared to the general population. Unfortunately none of the health benefits seen with the introduction of antiretroviral therapy have changed this figure, and paradoxically by increasing life expectancy the drugs may actually allow time for anal cancer to develop.

Infection with human papillomavirus (HPV or genital wart virus) is the most important risk factor for the development of anal pre-cancer and cancer. In 2007 the Pittsburgh AIDS Center for Treatment (PACT) instituted an anal cytology screening system where HIV-positive MSM were given anal Pap smears, and the anal cells collected were examined for any form of abnormality related to infection with HPV. To date, more than five hundred men have been screened and five cancers have been detected. For the over eighty men diagnosed with pre-cancer, an office based treatment procedure is available.

As the Pitt Men's Study (PMS), as part of the Multicenter AIDS Clinic Study (MACS), enters its next grant cycle, investigators - including those from Pittsburgh – have worked to address the issue of anal cancer development in both the PMS and the MACS-wide cohort of MSM. The Study has established itself as a unique source in the HIV epidemic to address research issues that demand long term follow up in both HIV-positive and HIV-negative men.

Because anal cancer likely develops in a stepwise fashion with increasingly abnormal cell types over a period of time, the Study could potentially provide answers to questions such as; what is the length of time to develop a pre-cancerous lesion? What is the effect of HIV viral load on progression of anal lesions? Is there a way in which to predict who will progress? And very importantly, what do the Study participants think of both the procedure and the test?

This research will be rolled out MACS wide, with the PMS offering sub-studies to address specific research questions. For the main study there will be one anal swab administered each year for HIV-positive participants and every other year for HIV-negative participants. There will also be an optional HPV swab at the intervening visits. Any participant with abnormal anal cells will be referred via their primary care physician for further assessment.

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Meet Your Researcher - James Becker

As a Pitt Men's Study volunteer, you are more to us than just handsome individuals. You are also a valuable source of data. Every vial of blood that we draw, personal question that we ask, and mental test that you suffer through is compiled and utilized by many different researchers.

Here and in the next few issues of the newsletter, we hope to introduce you to some of the men and women behind the curtain.

Red, blue, green, blue, blue, red… If those colors mean anything to you – or maybe even cause you to tear out your hair in frustration – chances are you've participated in neuropsychological testing at one of your recent Pitt Men's Study visits.

The man behind those neuropsych tests is James T. Becker, a professor of psychiatry, neurology, and psychology at the University of Pittsburgh School of Medicine. Since 1987 he has been a co-investigator for the Pitt Men's Study (PMS). Connecting dots, memorizing word lists, putting pegs in holes – we recently sat down with Dr. Becker to have a talk about what it all means.

Is there anything in particular that you're looking for in these data?

Over the last couple of years the PMS has really taken on a leadership role in the study of the brain. Some of the volunteers will be aware that we have been doing MRI scanning. That study was initiated here at Pitt, the data come here, the data are analyzed here.

One of the things I'm doing at the moment is finalizing a poster for the Academy of Neurology and simultaneously finalizing the resubmission of a manuscript to the Journal of Neurology, all based on data from men at the Pitt Men's Study.

We have a presentation I'm about to make in Toronto at the American Academy of Neurology where we looked at another measure of brain health using those MRI data, showing something I think the men already know but which is worth reinforcing, which is now that we've got the highly active drug therapies, a lot of other general health variables are becoming important.

For what do you use the data you get from tests like connecting the dots, or matching numbers with symbols?

At the end of 2009 we published a paper where we took advantage of all the trail making, digit symbol data that we've got over the last twenty-five years, as well as the detail testing [i.e. word memorization, etc]. We were able to find about 650 men across the entire MACS who were taking part in the cardiovascular study, and we looked at the relationship between variables associated with HIV disease, their cardiovascular health and their cognition. We looked specifically at memory and at psychomotor speed, which is sort of a measure of the brain's speed of processing, how everything moves.

What was striking was that the measures the MACS had taken about the health of your blood vessels, your heart, your arteries, your kidneys – the data were telling us that this was way more important to brain health than HIV disease. And it's not surprising because that's what everybody else has to deal with.

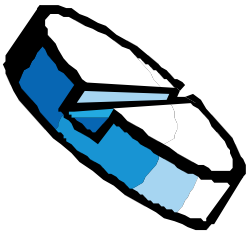
This is one of the things that as clinicians and researchers we have to keep reminding ourselves of. Ten or fifteen years ago there was this big eight hundred pound gorilla of HIV that you were trying to fight off, now you've got it tamed – it's not cured, but to a large a large extent, it's tamed. And now you've got all this other stuff running around which we forgot about. And the problem is that it's dangerous to forget about it because it is cumulative.

Can you talk about the importance of the volunteers to your research?

We could never have made any of the statements we are making now without the HIV-negative guys. We tend to focus on the guys with infection, and tend to think about focusing on the virus, but if you're going to talk about general health problems, you've got to have a good representation of everybody. The seronegatives are critical, and having them come back year after year, I know it's a pain in the neck, but it's critically important for us. When I write a sentence that says "We did MRI scans on people on who we have twenty-five years of clinical information," do you know how many jaws just drop? Nobody else has those data.

Alcohol and Drug Use and HIV Medications

by Rodger L. Beatty, PhD LSW



I never gave much thought of possible connections between HIV medications and use of alcohol or other illicit drugs. Sure, there was the obvious notion that if people with HIV were using alcohol or illicit drugs they might have problems with maintaining a medication schedule or simply just remembering whether they took their dose. What does research have to tell us about all of this?

In a 2002 study (McCance-Katz, et. al.) found that those taking Methadone, LAAM or buprenorphine for maintenance treatment of opioid addiction did not affect nelfinavir concentrations. While no toxicities were observed, they report that clinicians should be aware of the potential for drug interactions when patients require treatment with nelfinavir and these opiate medications. Antoniou and Tseng (2002) conclude that interactions between agents commonly prescribed for patients with HIV and recreational drugs such as MDMA, GHB, PCP, LSD can occur and may be associated with serious clinical antiretroviral efficacy and increasing risk of drug toxicity.

Harrington and colleagues report that most antiretroviral medications are also potent inhibitors (and occasionally inducers) of liver and intestinal system and therefore have the potential to alter the elimination of any substance that utilizes these metabolic pathways. They describe a patient with HIV-1 infection who was treated with ritonavir and saquinavir and then experienced a prolonged effect from a small dose of MDMA (ecstasy) and a nearly fatal reaction from a small does of GHB.

The most common drug interaction occurs when the body metabolizes drugs and that is the primary work of one's liver. In particular, protease inhibitors (the staple of most HIV medication doses) slow down how quickly the liver may clear other medications.

Remember those days when you were waiting in line to see a movie or favorite concert and some bullies pushed their way to the front of the line? Medications wait in line, too, to be cleared by the liver. They often compete with one another to get cleared. Protease inhibitors such as ritonavir (Norvir) are stronger and often win the battle. Therefore, the second medication in line is not cleared as quickly, likely resulting in an increased level of that drug within the blood. Some medications can even speed up how other medications are cleared by

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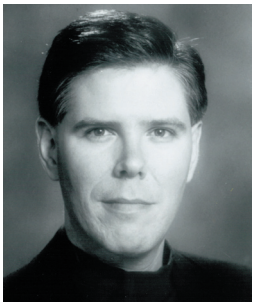
Congrats, Bill!



Everyone's favorite Pitt Men's Study clinic coordinator, Bill Buchanan, recently celebrated twenty-two years of working here! PMS co-investigator Tony Silvestre had this to say:

"Bill is at the very center of the Pitt Men's Study. Our study would be nothing if our men did not continue to participate and if the data were not collected correctly. He makes sure that both of those things happen. Plus we all love Bill."

Principle investigator Charles Rinaldo said: "Our study deals with a deadly disease afflicting the gay community. Bill is the direct link of the Pitt Men's Study to our hundreds of active volunteers. His loving and caring approach to our study volunteers provides the glue that keeps the study together and on the right track. I am certain that many of our volunteers have kept coming in for their clinic visits over the years because of their appreciation for being treated with such respect and concern by Bill."

The next time you see Bill, be sure to wish him a happy anniversary!

Alcohol and Drug Use and HIV Medications

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the liver. That is, if the second medication is cleared faster, there may not be enough of that medication left in the bloodstream to do its work. HIV medications being removed from the bloodstream too soon could lead to viral resistance, limiting the positive effects of these medications.

Although there appears to be no direct effects between alcohol use and HIV medications, chronic use of alcohol can certainly result in an overworked liver and kidneys. We know that nevirapine (Viramune) and D4T (Videx) will challenge a damaged liver, and that ddI (Zerit) will challenge a damaged pancreas. In addiction, chronic use of alcohol can lead to neuropathy (a numbness, sometimes painful, condition of the hands, feet and legs) which is made worse by ddI, D4T and ddC (Hivid). There are prescription sedatives such as Valium, Halcion, and Restoril as well as drugs such as GHB (sometimes called the "date rape drug") that, like alcohol, suppress the central nervous system (CNS). The combination of multiple CNS depressants has a potential for leading to seizures, difficulty breathing and with GHB, a possible coma.

No definite relationship has been shown between cocaine use and viral load. However one test tube study does suggest that cocaine use may cause HIV to replicate itself 20 times faster.

There is a theoretical concern that protease inhibitors, particularly ritonavir, can decrease the clearance of crystal methamphetamine from the body. This could possibly lead to a 2 to 3-fold buildup of crystal in the blood, thereby leading to an overdose. In addition, long term use of crystal meth can lead to weight loss, poor nutrition, and lack of sleep and fatigue, which might cause further damage to one's immune system.

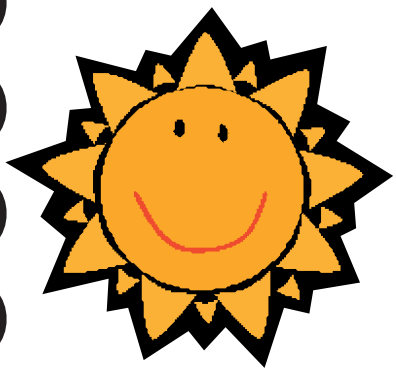
Likewise antiretrovirals, particularly ritonavir and delavirdine, may cause a 3- to 10-fold increase in Ecstasy levels, creating the potential for an overdose. Ironically, protease inhibitors such as ritonavir may decrease heroin levels by as much as 50%, thus reducing the possibility of a heroin overdose. However, that may lead a heroin addict to inject even more heroin to get the same effects. Naturally, if injection drug users do not use clean needles and works every time they inject, they run a greater risk for becoming re-infected with other strains of HIV (not to mention hepatitis viruses and other nasty microbes).

If you are taking highly active antiretroviral treatment (HAART) medications, you should seriously consider your use of alcohol, prescribed medications and illicit drugs. As always you should talk with your primary doctor about your challenges adhering to your HIV treatment regimen. Much of this information is from the AIDS Survival Project, Georgia's statewide resource for community-based advocacy and HIV treatment education: http://www.aidssurvivalproject.org. And, as always, please feel free to contact the Pitt Men's Study if you have further questions.

Antonius T and Tseng AL (2002) Interactions between recreational drugs and antiretroviral agents The Annals of Pharmacotherapy, 36 1598-1613

Harrington RD, Woodward JA, Hooton Thomas M and Hooton John R (1999) Life-threatening interactions between HIV-1 protease inhibitors and the illicit drugs MDMA and hydroxybutyrate Archives of Internal Medicine, 159, 2221-2224

McCance-Katz EF, Gourevitch MN, Arnsten J, Sarlo J, Rainey P and Jatlow P (2002) Modified directly observed therapy (MDOT) for injection drug users with HIV disease. American Journal of Addictions, 11, 271-278



PMS at Pride!

The Pitt Men's Study will have a table set up downtown at PrideFest on June 13, 2010. We'll be dispensing information, condoms, lube, free stuff and hugs, if you want them.
So come out and see us!