

aids treatment update

Alcohol & HIV

Whether you are living with HIV or not, some life-long vices - such as smoking or doing drugs - are not going to be good for your long-term health, even if you do them in moderation. But what about drinking?

In the UK, the idea of not drinking at all (being "teetotal") is regarded with some suspicion in a culture that celebrates everything from New Year's Eve to "after work" with a drink or three. And yet, studies have shown that people with HIV are more likely both to drink and to have problems with alcohol.

There is so much conflicting information regarding the risks and benefits of alcohol consumption that it can be difficult to make informed choices, particularly at this time of year, when we are faced with the temptation, and opportunity, to drink more than usual. Our lead article, 'Drink and be wary,' attempts to separate the fact from the fiction and help you understand how alcohol and HIV interact.

If you are struggling with trying to find the balance between enjoying life and staying healthy, then 'The Ikea approach', an extract from NAM's forthcoming 'Living with HIV' book, may help you find the ideal solution.

Here's wishing you a happy Festive Season, and a healthy New Year.

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drink and be wary

2 what happens when alcohol and HIV mix? asks edwin j bernard

Alcohol is the most widely-used recreational drug among both the general population and people with HIV. This time of year, most of us will be drinking more than usual. Besides giving us a monumental hangover on New Year's Day, will this be doing people with HIV any short- or long-term harm? And could the so-called 'heart healthy' benefits of a glass of red wine a day also be beneficial for HIV-positive people, who, whether on anti-HIV therapy or not, are more prone to heart disease?

Alcohol, HIV and the immune system

Scientists have looked at the effects that alcohol has on the non-HIV-infected immune system. They have found that, in the test-tube, alcohol can affect a variety of immune responses. It can reduce white cell counts, impairing immune function and antibody response, and increasing natural killer cell activity¹. However, the relationship between alcohol and the immune system is complicated and scientists cannot agree about whether drinking alcohol in moderation is harmful or not.

Most of the test-tube research that has examined the effect of alcohol on an HIV-infected immune system has used quantities of alcohol that would be equivalent to heavy or 'binge' drinking. Two years ago, scientists found that large quantities of alcohol may accelerate HIV disease progression by blocking a chemical messenger in the immune system and stimulating expression of the CCR5 co-receptor, which is used by HIV to infect cells².

Earlier this year, scientists found that HIV and alcohol may work together to suppress the immune system by weakening the activity of macrophages (white blood cells that roam body tissues, engulfing foreign organisms). But they

also discovered that large quantities of alcohol can suppress HIV replication. Overall, though, it seems that alcohol is more toxic to the immune system than it is to HIV – the researchers concluded that heavy alcohol use does appear to harm the immune system, and thus may lead to faster disease progression³.

What's in a unit?

In the UK, a unit is equal to 8g of alcohol. A unit is often defined as one 125ml glass of wine, half a pint of beer or lager or one pub measure of spirits. However, the alcohol content of some products is greater than it was 20 years ago when the unit system was devised. Today, the average wine glass size is 175ml and, at 13% alcohol by volume (ABV), a typical glass of wine would contain 2.3 units of alcohol. A half pint of beer is one unit if the ABV is 3.5%, but most are stronger than this, and a pint could easily contain 2.8 units.

Alcohol and HIV disease progression

Despite test-tube evidence of a possible relationship between alcohol use and HIV disease progression, prior to the widespread use of highly active antiretroviral therapy (HAART), no association between alcohol use and HIV disease progression had been found when scientists studied heavy drinkers living with HIV⁴. This is probably because untreated HIV is more damaging than even chronic, heavy alcohol use.

However, now that more individuals with HIV are living longer, new issues related to alcohol use and HIV, such as taking anti-HIV medicine on time and as prescribed (adherence), liver disease and hepatitis B and C co-infections,

have emerged. Researchers have found that good adherence to HAART is less often achieved in patients who have alcohol problems⁵. In recent years, hepatitis B and C have become increasingly common HIV co-infections. It has been established that since alcohol alone causes liver inflammation and can worsen hepatitis-related liver problems, alcohol use, HIV and, especially, hepatitis C combined can be a particularly problematic cocktail⁶.

Several studies have looked at whether alcohol worsens HIV disease progression in people on HAART. In 2000, Italian researchers⁷ compared CD4 cell counts and HIV viral load levels in non-drinkers, moderate drinkers (those drinking less than 60g of alcohol a day, equivalent to just over half a bottle of wine) and heavy drinkers (more than 60g a day) receiving HAART. They found that there were no differences in CD4 cell counts or viral load levels between the three groups.

At first glance, this appears to conflict with recent US research, which found that people on HAART with a history of alcohol problems who drank even the smallest amount of alcohol had higher viral loads and lower CD4 cell counts than those who did not drink⁸.

The most likely reason for the differences in the results of these two studies is that the Americans looked at individuals with a history of alcohol problems, whereas the Italian study did not mention whether participants had problems with alcohol. This suggests that it may be problems related to alcoholism or alcohol abuse (such as poor adherence or not eating well) rather than alcohol consumption itself that affected CD4 levels and viral loads. In fact, several studies have associated heavy alcohol use with poor adherence to anti-HIV medicines⁹ as well as with poorer response to HIV therapy in general.

However, another American study, published last year¹⁰, looked at the impact of different levels of drinking on the CD4 cell counts, HIV viral loads and nutritional status of 220 HIV-positive drug users (crack, cocaine and cannabis were the most commonly-used drugs). It found that the heavy drinkers (for this study, those drinking alcohol three to four times a

week) were more likely to be malnourished, were twice as likely to have a CD4 cell count below 500 cells/mm³ and were four times less likely than light and non-drinkers to achieve an undetectable viral load. The researchers suggested that several factors could be responsible for this difference, including poor adherence, poor drug absorption and drug interactions. The latter two factors may be due to the fact that many anti-HIV drugs are processed by the same liver enzyme that processes alcohol.

How much is moderation?

UK Health Agencies recommend that healthy men should not drink more than 3 to 4 units of alcohol per day. For healthy women, the daily limit is 2 to 3 units. This advice applies regardless of whether you drink daily, weekly or somewhere in between. Women who are pregnant, or planning to become so, are advised to drink no more than 1 to 2 units per week. There are no guidelines for people living with chronic illnesses such as HIV disease.

Alcohol, HIV and the liver

Alcohol has the potential to impact on the way the liver processes (metabolises) anti-HIV medications. Although no serious or interactions have been seen to be caused by drinking alcohol at the same time as taking any anti-HIV medicine, significant interactions can still occur depending on how well an individual's liver is functioning and how much alcohol they are drinking¹¹.

Current British HIV Association (BHIVA) guidelines on hepatitis and HIV co-infection suggest that anyone living with HIV and hepatitis B should practice "abstinence or limited use of alcohol" if they have abnormal liver test results. However, BHIVA recommends that people co-infected with HIV and hepatitis C should abstain from alcohol completely.

In hepatitis C-only infected individuals, an increased risk of liver scarring (cirrhosis) is associated with sustained alcohol consumption of greater than 50g each day. However, a recent study found that drinking less than 50g of alcohol a day did not seem to make the liver disease associated with chronic hepatitis C infection

If you're worried about the negative effects of alcohol on either yourself or someone else, Alcohol Concern offers an excellent service: visit www.alcoholconcern.org.uk.

References

1. Szabo G et al. *Alcohol & Alcoholism* 34(6): 830-841, 1999.
2. Wang X et al. *Alcoholism, Clin Exp Res* 26(12): 1880-1886, 2002.
3. Haorah J et al. *Cell Immunol.* 229(2): 139-48, 2004.
4. Dingle GA, et al. *Psychol Bulletin* 122: 56-71, 1997.
5. Fabris P et al. *JAIDS* 25: 92-93, 2000.
6. Martin-Carbonero L et al. *Clin Inf Dis* 38(1): 128-133, 2004.



significantly worse. The scientists concluded that light or moderate drinking might have only a minimal, or even no effect, on liver scarring. However, this study did not include people co-infected with hepatitis C and HIV¹².

Drug interactions

Although it has been discovered that alcohol can increase blood levels of the nucleoside analogue anti-HIV drug abacavir (*Ziagen*, also found in *Trizivir* and *Kivexa*) by up to 40%, this increase is not considered to be a problem unless you already have moderate or severe liver disease¹³.

The nucleoside analogue anti-HIV drug ddI (*Videx* and *VidexEC*) and drinking large quantities of alcohol can each by themselves increase the risk of pancreatitis. Symptoms include the sudden onset of abdominal pain, fever, vomiting or general worsening of health. If ddI-related pancreatitis does develop, alcohol should be strictly avoided.

Alcohol can also interact with the nucleoside analogue anti-HIV drug AZT (zidovudine, *Retrovir*, also found in *Combivir* and *Trizivir*), and this may interfere with an enzyme called thymidine kinase¹⁴. However, no unexpected effects on AZT's potency have been reported in clinical practice.

There is a particular problem with the antibiotics metronidazole and tinidazole, which cause an unpleasant reaction when taken with alcohol. In addition, alcohol can interact with many common prescription and over-the-counter medicines, particularly those which carry the warning 'may cause drowsiness'. It can be dangerous if consumed with some types of antidepressants, tranquilisers, sleeping pills, some antihistamines or certain types of opioid (morphine-like) pain relievers such as dihydrocodeine or co-proxamol. Ask your pharmacist if you are not sure whether drinking alcohol with your medicines could cause problems.

HIV, the heart and alcohol

Last year's landmark DAD (Data collection on Adverse events of anti-HIV Drugs) study reported a 26% increased risk in the frequency of heart attacks per year of

Alcohol and HIV transmission

Behavioural studies have found a connection between being drunk and having risky sex. However, it is not only alcohol's effects on behaviour that make getting drunk a riskier affair as far as HIV transmission is concerned. Last year, a study using rhesus monkeys and SIV (the simian version of HIV) found that, one week after infection, alcohol increases the amount of viral replication by 60 times. The researchers suggest that this could mean that people who drink a lot could be more susceptible to becoming HIV infected¹⁵. Another recent study suggests that alcohol may influence HIV transmission through oral sex because it stimulates the production of CXCR4 (a co-receptor that is used by HIV to infect cells) in the mouth¹⁶.

antiretroviral drug exposure. This year, they added strokes and heart bypass operations to the increased-risk list¹⁷. Another study found that being infected with HIV itself increases the risk of heart disease¹⁸.

A number of studies in non-HIV-infected people have shown that no more than three units of alcohol for men and two units for women per day appears to lower the risk of heart attack for people in middle age by roughly 30%-50%. If you are younger than 35, then taking HAART probably increases your heart attack risk to that of someone who is middle-aged, and therefore, this low-moderate amount of alcohol (along with stopping smoking, eating a heart-friendlier diet and exercising regularly) might help reduce that risk.

Studies also suggest that this same low-moderate alcohol consumption can reduce your risk of stroke and other coronary artery diseases. The studies indicate that alcohol can raise the amount of high-density lipoprotein (HDL) cholesterol (the "good" cholesterol) in your body. HDL removes "bad" cholesterol from your arteries, lowering your risk of atherosclerosis – the accumulation of fatty deposits (plaques) in your arteries¹⁹.

In addition, HDL cholesterol is known to have a role in immune response. Apolipoprotein A1, a component of HDL cholesterol, inhibits herpes simplex and also has some inhibitory effect on HIV. Last year, a Spanish study²⁰ found that higher levels of HDL cholesterol were associated with better reductions in viral load when taking anti-HIV drugs.

There is no agreement, however, on whether wine is better for you than beer or spirits. Some studies suggest that red wine is better for you because it contains such beneficial compounds as the potent anti-oxidant, resveratrol. Other studies document the same cardiovascular benefits for all types of alcohol.

Alcohol and lipodystrophy

People with HIV who are taking anti-HIV regimens that are likely to cause high blood fat levels and fat redistribution problems may want to consider the extent to which excessive alcohol consumption can cause central fat accumulation. It is increasingly agreed that central fat accumulation is caused by insulin resistance, and one of the main ways in which excessive alcohol increases the risk of heart disease is by increasing insulin resistance. One study²¹ found that high levels of alcohol consumption were associated with the highest "bad" cholesterol levels, although another²² found that there was no relationship between any amount of alcohol and the fat gain associated with lipodystrophy.

'Binge drinking'

In 1995, the Government changed the guidelines for sensible drinking. The new figures give daily, not weekly, recommended maximum quantities. This reflects official concern over the phenomenon of 'binge drinking', which is defined as eight or more units for men and six or more units for women on at least one day in the week. Most worrying for HIV-positive people is the way 'binge drinking' negatively affects behaviour – this can lead to increased vulnerability to sexual or physical attack, for example, or to forgetting to take anti-HIV medicines or practising riskier sex than when sober. However, there are health problems directly attributed to 'binge drinking', too. A recent study²³, presented at the American Heart

Association meeting in November, found that the risk of developing metabolic syndrome (a cluster of cardiovascular disease risk factors including high blood pressure, elevated triglycerides, low levels of (HDL), impaired fasting glucose and excess abdominal fat) in HIV-negative people increases the more a person drinks, and that beginning a heavy drinking pattern early in life seems to add extra risk. The researchers concluded that it is healthier to drink smaller amounts per drinking day than to drink more on fewer days, in line with current guidelines on moderate drinking. "The drinking pattern of one drink per day is much healthier than seven drinks on a weekend," lead author Amy Fan told the conference.

A balanced approach

Alcohol is a major contributor to ill-health and disease in the UK, and leads to greater loss of life than any other recreational drug, legal or not. Because of its power to alter mood and make physical changes, it can also lead to physical, psychological and social problems. In addition, alcoholism is a widespread problem in the UK. Heavy drinking can affect the immune system, may slow down recovery from infections, and may lead to faster disease progression. 'Binge drinking' can lead to poor co-ordination, exaggerated emotional reactions and eventually, if unchecked, to unconsciousness and possibly coma and death. Long-term consumption of large quantities of alcohol can lead to liver damage, heart disease and brain damage.

However, moderate drinking relaxes the nervous system and leads to a pleasant and uninhibited feeling. Many people find that having a couple of drinks helps to relieve feelings of stress or anxiety. Since moderate drinking is also linked to a reduced risk of heart disease, few UK doctors would advise their HIV-positive patients to give it up, unless they were also co-infected with hepatitis C, or were abusing alcohol to an extent that was causing harm.

7. Fabris P, et al. JAIDS 25: 92-93, 2000.
8. Lucas, G.M et al. AIDS 16(5): 767-774, 2002.
9. Wagner, J.H et al. J Clin Epidemiology 54(12) Suppl. 1: S91-S98, 2001.
10. Miguez MJ et al. Addiction Biology 8: 33-37, 2003.
11. Kresina TF,et al. AIDS Res Hum Retroviruses 18: 757-770, 2002.
12. Monto A et al. Hepatology 39: 826-834, 2004.
13. McDowell JA et al. Antimicrob Agents Chemother 44: 1686-1690, 2000.
14. Prakash O et al. 24th Annual Scientific Meeting of the RSA, Montreal, abstract 123, 2001.
15. Bagby GJ et al. Alcohol Clin Exp Res. 27(3): 495-502. 2003.
16. Chen H, et al. AIDS Res Hum Retroviruses 20(5): 513-9, 2004.
17. The DAD Writing Committee. AIDS 18: 1811-1817, 2004.
18. Currier J. JAIDS 33: 506 - 512, 2003.
19. Vogel RA. Reviews In Cardiovascular Medicine 3(1), 2002.
20. Alonso-Villaverde C et al. AIDS 17: 1173 - 1178, 2003
21. Hadigan C et al. Clinical Infectious Diseases 33: 710-7, 2001.
22. Hendricks KM et al. Am J Clin Nutr 78: 790-5, 2003.
23. Fan AZ et al. American Heart Association Meeting, New Orleans, abstract 3842, 2004.

the ikea approach

6 the swedish furniture store provides unlikely inspiration for *ATU* reader and 'Living with HIV' contributor john moon.

Editor's note: Life with HIV in the UK has changed dramatically during the past nine years. Where once we dealt with death, and then wondered with amazement at how new treatments were bringing people back from the dead, now we deal with HIV issues that were as-yet unthought-of in 1996: pensions, planned parenthood, which anti-HIV combination best fits our lifestyle, whether to take anti-HIV drugs at all.

Consequently, the time was ripe for NAM to completely update our book 'Living with HIV', last published in early 1996, just before effective anti-HIV treatments became available. Early next year, the new 'Living with HIV' book will be made available free to anyone living with

HIV in the UK. It is hoped that the book will contain something useful both for people who have been recently diagnosed with HIV and for those who have known that they have had HIV for some time.

The ideal way to use the book, says editor Michael Carter, "is to keep it on your bookshelf and dip into it as and when needed."

Like the first edition, the new 'Living with HIV' is liberally peppered with personal testimonies from NAM subscribers and *ATU* readers, providing first-hand information and inspiration regarding the various challenges that HIV brings each day. To whet your appetite for the book, here is one of my favourites: 'The Ikea Approach'.

I've no doubt that the main reason that I'm alive and well after almost 14 years of living with HIV is because combination therapy became available in 1996, just as my immune system was starting to become so weak that I was vulnerable to AIDS-defining illnesses.

Well, eight years on, my T-cell count is over 1,000 and my viral load has been undetectable for years.

But as well as acknowledging how important HIV drugs have been, I also want to claim a bit of the credit for doing my bit to keep myself healthy and fit. It's what I call my "Ikea approach" (after the low-cost Swedish home furnishing store that keeps prices down by asking customers to collect their purchases from the warehouse, and assemble them themselves). Well, I met the medicines half-way by making sure I looked after myself.

First of all I make sure I take my anti-HIV pills. Okay, I've missed the odd dose, and taken some a few hours late. But I seem to have got away with it and am still taking my first combination (except for one change due to side-effects).

Then there's my diet. For the first few years after my HIV diagnosis I was obsessive about my diet, making sure that my diet, from my bowl of wholemeal porridge for breakfast, to my fruit salad desert after supper, was as healthy as possible. It may have been healthy, but it was also very worthy and, actually, boring. I'm now much more relaxed and more or less eat what I want, particularly as I once heard an HIV doctor say that being HIV-positive means "eating for two". Okay, I still make sure that I eat lots of fresh fruit and veg, and am easy on the lard, but now I allow myself food that I want to eat, not food that I feel I should eat.

I've always been pretty active and do a lot of exercise. Being honest, vanity was my main motivation to start off with - I found it was much easier to pull off with a few muscles - but over the years, fitness and health has become more of a priority. I do a blend of weights and cardio and hope that's helped control my blood fats even though I'm taking a protease inhibitor.

At times I've used complementary and alternative treatments. For a few years, in the early 90s, I was actually quite into them. There seemed to be so little else I could do to fight HIV. I tried a few things, including acupuncture, high dose vitamins and Chinese herbs. Well, my T-cell count didn't go down when I was using them, but they still didn't prevent me getting a bad chest infection which meant a lengthy stay in hospital.

I do still use them though, but am realistic about what they can achieve. As far as I'm concerned, anti-HIV drugs are the reason I'm alive and well, the complementary stuff is just that - a desirable add-on, to help me feel more comfortable. Acupuncture helps me relax, and really did help to relieve the side-effects I experienced when I started my first combination. The odd massage makes me feel better, and I still take a multivitamin every morning. I figure it can't do me any harm, and might actually do me some good.

Having got my life back, I want to enjoy it. That hasn't always been easy. I've gone through some really bleak periods during the time I've had HIV and actually felt suicidal at times. Counselling helped at times, but at others talking about feeling bad and why I felt awful actually made things worse! Antidepressants helped a lot, though, as did some focused psychotherapy when I wasn't actually depressed.

Since I was a student, I've enjoyed a drink, and still do. I've also had some great times on drugs of various descriptions. Projectile vomiting and convulsing in a club after taking a pill a few months after starting HIV medicines was a bit of a wake-up call and I haven't touched anything since. I know a lot of people manage to mix medicines and recreationals, but that was just too frightening for me.

Just after my HIV diagnosis I bought a sofa from Ikea, thinking that as I wasn't going to last too long, it didn't matter if it didn't either. Well, the sofa, like me, is still here.

news from ICAAC

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The 44th Interscience Conference on Antimicrobial Agents & Chemotherapy (ICAAC) took place last month in Washington DC. This annual meeting of the American Society for Microbiology is one of the year's biggest scientific meetings concerning HIV and AIDS and some important new information was reported here for the first time.

***Kaletra* loses potency in very hot climates**

The quality and the potency of Lopinavir/ritonavir (*Kaletra*) capsules are likely to deteriorate in hot climates, according to researchers from the United States National Institutes of Health. Although *Kaletra's* manufacturer, Abbott Laboratories, has shown that capsules are stable and potent for two months when stored at 25°C, it's a different story at temperatures of 35°C and 45°C. After a day at 45°C, the capsules became soft, sticky and broke apart when separated from each other. Although the drug content remained above 95% at both temperatures up to day 30, it had fallen below the acceptable limit of 85% by day 60, indicating that the drug might no longer be effective – even if patients were able to separate capsules from each other in order to take the correct dose. The researchers recommend that Abbott should investigate storage of single capsules in blister packs to prevent clumping of capsules, and that no more than 30 days' worth of *Kaletra* should remain unrefrigerated at these temperatures.

Capparelli E et al. Stability of lopinavir/ritonavir (LPV/RTV) at elevated temperatures: relevance to HIV therapy in sub-Saharan Africa, abstract H-868.

Is tipranavir/ritonavir a better choice than other boosted PIs in salvage therapy?

Tipranavir boosted with ritonavir (*Norvir*) is about as twice as effective at reducing viral load to 'undetectable' levels as other commonly prescribed ritonavir-boosted protease inhibitors (PIs) in patients with extensive treatment experience, according to preliminary 24-week findings from the RESIST-1 study. However, 7% of people on tipranavir experienced significant liver enzyme elevations compared to 1% of people on other boosted PI combinations. Significant increases in cholesterol and triglyceride levels were also more common in people on tipranavir. Tipranavir is a new PI developed by Boehringer Ingelheim that is dosed twice daily with 200mg of ritonavir. It is expected that a European license will be granted by summer 2005.

Hicks C et al. RESIST-1: a phase 3, randomized, controlled, open label, multicenter trial comparing tipranavir/ritonavir (TPV/r) to an optimized comparator protease inhibitor/r (CPI/r) regimen in antiretroviral (ARV) experienced patients: 24 week data, abstract H-1137a.

Trizivir + tenofovir provides new treatment choices

For people who are taking anti-HIV therapy for the first time, a combination of four drugs in just three pills a day (tenofovir (*Viread*) with *Trizivir* which contains AZT, 3TC and abacavir) appears to be as effective and tolerable as the three pills a day anti-HIV regimen of *Combivir*, which contains AZT and 3TC, and efavirenz (*Sustiva*). *Combivir* plus efavirenz is currently the most commonly prescribed first-line regimen in the United Kingdom. Last year, British treatment guidelines warned that *Trizivir* should not be used alone, even though it contains three drugs, after several trials were stopped early when people taking *Trizivir* alone did much worse than people taking other triple drug combinations. However, adding tenofovir appears to be not only safe and effective, but also leaves more options open for future treatment if or when that combination fails, since all four drugs are of the same broad class. In a separate, preliminary, report published halfway through a 48-week study, *Trizivir* and tenofovir were said to be looking like an effective and well-tolerated second-line regimen in individuals who had experienced early treatment failure with either a non-nucleoside-based or protease inhibitor-based initial combination.

Moyle G et al. A randomised open label comparative study of Combivir and efavirenz (two class triple therapy) versus Trizivir and tenofovir (single class quadruple therapy) in initial therapy for HIV-1 infection, abstract H-1131.

Rodriguez AE et al. Abacavir/lamivudine/zidovudine and tenofovir in subjects with early virologic failure on an initial regimen of zidovudine or stavudine and lamivudine and a protease inhibitor or non-nucleoside reverse transcriptase inhibitor (ESS3005, ZIP), abstract H-563.

Kaletra exposure decreased by tenofovir in experienced HIV patients

Antiretroviral-experienced HIV-positive patients taking lopinavir/ritonavir (*Kaletra*) at the same time as tenofovir (*Viread*) may require increased doses of *Kaletra* to achieve adequate drug levels. Although previous studies have

shown that tenofovir has only a small effect on blood levels of *Kaletra*, this new study was restricted to treatment-experienced HIV-positive patients, and found significant reductions in drug concentrations of lopinavir in the blood. Although no-one knows why this happens, the researchers suggest that drug level monitoring for treatment-experienced patients on both *Kaletra* and tenofovir will help doctors choose the appropriate dose of *Kaletra*, which may need to be increased from three capsules twice daily to four capsules twice daily.

Breilh D et al. Pharmacokinetic drug interaction of lopinavir/ritonavir in combination with tenofovir in experienced HIV+ patients, abstract A-445.

Efavirenz not associated with long-term depression

Efavirenz (*Sustiva*) has been suspected of causing long-term depression that persists in a minority of people beyond the well-documented central nervous system side-effects, like dizziness and sleep disturbances, commonly seen in the first month on therapy. However this link is controversial. A new study that compared people who remained on their successful PI-based anti-HIV regimen with people who switched to an efavirenz-containing regimen has found that the only significant factor associated with depression and suicidal thoughts when on efavirenz is a previous history of depression.

Journot V et al. Risk of depression or suicide among HIV-infected patients in a trial comparing maintenance of a protease inhibitor-containing regimen with the switch to a once-daily efavirenz+ddI+FTC, abstract H-167.

Men shed HIV more often than women

Men more frequently have detectable HIV in their sexual fluids than women, meaning that men, even when taking highly active antiretroviral therapy (HAART) that is successfully controlling viral load in the blood, could be more infectious than women.

Coombs RW et al. A comparison of HIV-1 level in blood and non-blood compartments between men and women: baseline analysis of ACTG protocol A5077, abstract H-198.

AZT & d4T damage fat cells long before fat loss is visible

The anti-HIV drugs AZT (zidovudine, *Retrovir*) and d4T (stavudine, *Zerit*) begin to cause damage to fat cells long before physical signs of fat wasting appear, according to findings presented at the Sixth International Workshop on Lipodystrophy and Adverse Drug Reactions in HIV in Washington DC. In contrast, people taking abacavir (*Ziagen*) and 3TC (lamivudine, *Epivir*) showed no evidence of damage to fat cells.

Reference

Nolan D et al. Differential effects of nucleoside reverse transcriptase inhibitor (NRTI) regimens on adipocyte mitochondrial DNA depletion in HIV-infected patients. *Antivir Ther* 9: L11, 2004.



Hard drug use leads to more AIDS-defining illnesses

A US study of 1148 women, comparing non-drug-users to drug-users, has found that the use of cocaine, heroin or methadone, or the injecting of any drugs, led to 65% more AIDS-defining illnesses over a five-year period, but led to no significant changes in numbers of CD4 cells or levels of HIV. The most common AIDS-defining illnesses seen during the study were: herpes infections, pneumonias of various types and tuberculosis (TB). Pneumonia and TB were significantly more common among drug users. The investigators comment that these illnesses are common in drug-users in general and are often seen in HIV-positive people who have relatively high CD4 counts. Their prevalence among drug-users may therefore be caused by their exposure to disease-causing organisms via drug use, rather than by direct damage to their immune function caused by hard drugs. In addition, hard drug use did not lead to faster death. In fact, the only significant factor affecting death rates was the use of anti-HIV therapy, which reduced death rates by 80%. The investigators conclude from this study that use of hard drugs has no direct effect on the natural history of HIV, but can make people ill more often.

Thorpe LE et al. Effect of hard-drug use on CD4 cell percentage, HIV RNA level, and progression to AIDS-defining class C events among HIV-infected women. *J Acquir Immune Defic Syndr* 37:1423-1430, 2004.

Kaletra could worsen hepatitis B or C

HIV-positive individuals also co-infected with either hepatitis B or C viruses have a significantly increased risk of developing clinically significant elevated liver enzymes when taking a *Kaletra*-containing anti-HIV regimen, according to two recent studies. The first, a Canadian study presented at the International AIDS Conference in Bangkok, found that *Kaletra* (lopinavir/ritonavir) was significantly associated with the development of grade 3/4 elevations in liver enzyme levels in those people co-infected with hepatitis B or C. The second, an Italian study published last month, found that 16% of hepatitis B or C co-infected patients developed elevated liver enzymes compared to only 3% of patients without these infections. Most of the patients who stopped *Kaletra* due to its effects on their liver returned to their pre-*Kaletra* levels, however. These two studies emphasise the importance of both testing for hepatitis co-infection before starting anti-HIV therapy and monitoring liver function before and during therapy.

Meraviglia P et al. Lopinavir/ritonavir treatment in HIV antiretroviral experienced patients: evaluation of risk factors for liver enzyme elevation. *HIV Med* 5: 334-351, 2004.

Chihrin S et al. Exposure to lopinavir/r is a risk factor for grade 3 / 4 elevation of ALT in HIV and hepatitis B (HBV) and/or C (HCV) coinfecting patients. Fifteenth International AIDS Conference, Bangkok, abstract MoPeB3281, 2004.

Nevirapine significantly boosts 'good' cholesterol

More results from the 2NN study, which compared the two non-nucleoside anti-HIV drugs efavirenz (*Sustiva*) and nevirapine (*Viramune*), show that both drugs increase levels of high density lipoprotein (HDL) cholesterol (the so-called 'good' cholesterol) more than any protease inhibitor-containing regimen. However, nevirapine outshone efavirenz by a five-to-one margin; the investigators estimated that, based on the study results, taking efavirenz could reduce the risk of cardiovascular disease by 3% compared with protease-inhibitor-based regimens, whilst taking nevirapine could reduce the risk by 15%. The nevirapine risk reduction is similar to that of the most powerful lipid-lowering agents in the statin and fibrate classes, suggesting that taking nevirapine as part of an anti-HIV regimen may have particular benefits for HIV-positive people with multiple risk factors for heart disease that include low HDL cholesterol.

Van Leth et al. Nevirapine and efavirenz elicit different changes in lipid profiles in antiretroviral-therapy-naïve patients infected with HIV-1. *Public Library of Science Medicine* 1: e19, 2004.

Triple class drug resistance increase seen Europe-wide

Nearly 13% of people on anti-HIV therapy throughout Europe have resistance to all of the three main classes of antiretroviral drugs, according to a new report from the EuroSIDA study group. They found that the incidence of triple class resistance was similar in both treatment-naïve and treatment-experienced patients after five years, and that individuals with resistance to all the three main classes of anti-HIV drugs were significantly more likely to experience disease progression or death. "By 2003, one in 20 treatment-naïve and one in six treatment-experienced patients from the EuroSIDA study who started receiving HAART experienced triple class failure", write the investigators. They also draw attention to the

implications of triple class resistance for both patients and HIV clinics: "For the individual, this may lead to a poorer prognosis and to potential transmission of resistant virus to others. For the clinics, it may lead to increased cost due to more-intensive diagnostic tests, the use of more-expensive drugs such as enfuvirtide (T-20), and the use of more drugs in each regimen."

Mocroft A et al. Time to virological failure of three classes of antiretrovirals after initiation of highly active antiretroviral therapy: results from the EuroSIDA study group. *J Infect Dis* 190: 1947 - 46, 2004.

Roche drops 625mg film-coated nelfinavir tablet

Drug company Roche has announced that it is withdrawing its convenient 625mg film-coated tablets of the protease inhibitor nelfinavir (*Viracept*) due to "recurrent manufacturing difficulties". Although not fully approved through the European drug regulatory authorities, the 625mg tablet had received endorsement from the European Committee on Proprietary Medical Products and was available through expanded access and clinical trials. Roche will withdraw these within the next six months and the company suggests that people currently on the tablet should consider moving to the 250mg tablet. The 250mg tablet is not affected by any manufacturing difficulties and, says Roche, "remains an option in the therapy of HIV". However, since the usual recommended dose of nelfinavir is 1250mg twice daily, the daily drug burden for those who make the switch will increase from four to ten tablets.

Stop Press: Tenofovir/ddI: is CD4 cell loss on treatment linked to this combination?

The combination of tenofovir and ddI may result in unexpected declines in CD4 cell count, according to two Spanish studies presented at recent international conferences, but the phenomenon is not clearcut and needs further investigation, according to other findings presented at the Seventh International Congress on Drug Therapy in HIV Infection in Glasgow last month. ATU will examine this issue in detail next month.

news from nam

Are you a friend of NAM?

Caspar Thomson, NAM's director, has just written to you to ask you to support our final fundraising push this year. Please support NAM's work with just £10 a month and become a Friend of NAM. If you are already a supporter, please consider giving a little extra with a £25 donation. With your help, we can provide more people with free information resources, such as ATU and aidsmap.com, which help people live longer, healthier lives. If you haven't received a letter from Caspar and you want to support our work, call us on 020 7840 0065 and we'll do the rest.

Next year's ATU

The first issue of *AIDS Treatment Update* for 2005 will be a combined January/February double issue, which you should receive in the second week of January, postal deliveries permitting. Inside this bumper issue we will be looking forward to the new treatment options that will become available in 2005. We will also be looking at the longer-term choices available to people who have had their CD4 counts drop below 200 cells/mm³.

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