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ARV4IDUs

ANTIRETROVIRAL TREATMENT FOR INJECTING DRUG USERS: A QUARTERLY BULLETIN

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Antiretroviral Tretment for Injecting Drug Users: A quarterly bulletin

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ARV4IDUs is a not-for-profit community publication that aims to provide a review of the most important medical advances related to clinical management of HIV and its related conditions for injecting drug users, as well as access to treatments. Comments to articles are compiled from consultant, author and editorial responses.

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EDITORIAL

Welcome to the December 2010 issue of the HIV i-Base bulletin *ARV4IDUs*.

In this issue, you will find our coverage of the XVIII International AIDS Conference, 18-23 July 2010, Vienna, Austria. As usual, we take a look at the main areas of latest scientific research and development that are of particular relevance to HIV and IDUs.

We have also published the section on treatment of HIV in IDUs from the just-issued US DHHS guidelines. We hope that this important document will help both doctors and advocates in their work to improve the treatment and quality of life of HIV-positive IDUs.

We are happy also to welcome two new writers to our pages—Anastasia Solovyeva and Denis Godlevskiy. Anastasiya reports on hepatitis D (HDV), an often-neglected infection, but of huge importance when it comes to treatment of IDUs. In this issue we include coverage from the specialised HDV conference organised by the European Association of the Study of the Liver, held on 25-26 September in Istanbul, Turkey.

Denis analyses the specific problems of access to treatment for IDUs in the Russian Federation in connection with the interruptions of supplies of ARVs in different regions of the Federation.

We always like to encourage new writers and reviewers who would like to contribute to future issues. This can include research reports and overview articles. If you would like to contribute to future issues or have news to include, please email:

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GUIDELINES

US Department of Health and Human Services *Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents* publish a special section on HIV and IDUs

To recognise the importance of this document published in January 2011 and particularly taking into account its practical usefulness in certain settings, we include the whole section on treatment of HIV in IDUs.

http://www.aidsinfo.nih.gov/guidelines/

HIV AND ILLICIT DRUG USERS (IDUs) (Updated January 10, 2011)

Treatment Challenges of HIV-Infected IDUs

Injection drug use is the second-most common mode of HIV transmission in the United States. In addition, noninjection illicit drug use may facilitate sexual transmission of HIV. Injection and noninjection illicit drugs include the following: heroin, cocaine, marijuana, and club drugs (i.e., methamphetamine, ketamine, gamma-hydroxybutyrate [GHB], and amyl nitrate). The most commonly used illicit drugs associated with HIV infection are heroin and stimulants (e.g., cocaine and amphetamines); however, the use of club drugs has increased substantially in the past several years and is common among those who have HIV infection or who are at risk of HIV infection.

Methamphetamine and amyl nitrate (i.e., poppers) have been the most strongly associated with high-risk sexual behavior in men who have sex with men (MSM), and the association is less consistent with the other club drugs *[1]*.

All illicit drugs have been associated with depression and anxiety, either as part of the withdrawal process or as a consequence of repeated use. This is particularly relevant in the treatment of HIV infection because depression is one of the strongest predictors of poor adherence and poor treatment outcomes *[2]*. Although treatment of HIV disease in this population can be successful, IDUs who have HIV disease present special treatment challenges. These may include the following: (1) an array of complicating comorbid medical and mental health conditions; (2) limited access to HIV care; (3) inadequate adherence to therapy; (4) medication side effects and toxicities; (5) the need for substance abuse treatment; and (6) drug interactions that can complicate HIV treatment *[3]*.

Underlying health problems among injection and noninjection drug users result in increased morbidity and mortality, either independent of or accentuated by HIV disease. Many of these problems are the consequence of prior exposures to infectious pathogens from nonsterile needle and syringe use. Such problems can include hepatitis B or C virus infection, tuberculosis, skin and soft tissue infections, recurrent bacterial pneumonia, and endocarditis. Other morbidities such as alteration in levels of consciousness and neurologic and renal disease are not uncommon. Furthermore, these comorbidities are associated with a higher risk of drug overdoses in IDUs with HIV disease, due in part to respiratory, hepatic, and neurological impairments *[4]*. Successful HIV therapy for IDUs often rests upon acquiring familiarity with and providing care for these comorbid conditions and overdose prevention support.

IDUs have less access to HIV care and are less likely to receive antiretroviral therapy (ART) than other populations *[5-6]*. Factors associated with low rates of ART among IDUs include active drug use, younger age, female gender, suboptimal health care, recent incarceration, lack of access to rehabilitation programs, and lack of expertise among health care providers *[5-6]*. The typically unstable, chaotic life patterns of many IDUs; the powerful pull of addictive substances; and common misperceptions about the dangers, impact, and benefits of ART all contribute to decreased adherence *[7]*. The chronic and relapsing nature of substance abuse as a biologic and medical disease, compounded by the high rate of mental illness that antedates and/or is exacerbated by illicit substance use, additionally complicate the relationship between health care workers and IDUs *[8-9]*. The first step in provision of care and treatment for these individuals is to recognise the existence of a substance abuse problem. Whereas this is often open and obvious, patients may hide such behaviors from clinicians. Assessment of a patient for substance abuse should be part of routine medical history taking and should be done in a clinical, straightforward, and nonjudgmental manner.

Treatment efficacy in HIV-infected illicit drug use populations

Although IDUs are underrepresented in HIV therapy clinical trials, available data indicate that—when they are not actively using drugs—efficacy of ART in IDUs is similar to that seen in other populations [10]. Furthermore, therapeutic failure in this population generally correlates with the degree that drug use disrupts daily activities rather than with drug use per se [11]. Providers need to remain attentive to the possible impact these factors have upon the patient before and during prescription of ART. Although many IDUs can sufficiently control their drug use over long enough periods of time to benefit from care, substance abuse treatment is often necessary for successful HIV management.

Close collaboration with substance abuse treatment programs and proper support and attention to this population's special multidisciplinary needs are critical components of successful HIV treatment. Essential to this end are accommodating and flexible, community-based HIV care sites that are characterised by familiarity with and nonjudgmental expertise in management of drug users' wide array of needs and in development of effective strategies to promote medication adherence [9], including, if available, the use of adherence support mechanisms such as modified directly observed therapy, which has shown promise in this population [12].

Antiretroviral agents and opioid substitution therapy

IDUs are more likely to experience an increased frequency of side effects and toxicities of ART. Although not systematically studied, this is likely because underlying hepatic, renal, neurologic, psychiatric, gastrointestinal, and hematologic disorders are highly prevalent among IDUs. Selection of ARV agents in this population should be made with consideration of these comorbid conditions. Opioid substitution therapies such as methadone and buprenorphine/naloxone and extended release naltrexone are commonly used for management of opioid dependence in HIV infected-patients.

Methadone and ART. Methadone, an orally administered, long-acting opioid agonist, is the most common pharmacologic treatment for opioid addiction. Its use is associated with decreased heroin use, decreased needle sharing, and improved quality of life. Because of its opioid-induced effects on gastric emptying and the metabolism of cytochrome P (CYP) 450 isoenzymes 2B6, 3A4, and 2D6, pharmacologic effects and interactions with ARV agents may commonly occur *[13]*. These may diminish the effectiveness of either or both therapies by causing opioid withdrawal or overdose, increased methadone toxicity, and/or decreased ARV efficacy. Efavirenz (EFV), nevirapine (NVP), and lopinavir/ritonavir (LPV/r) have been associated with significant decreases in methadone levels. It is necessary to inform patients and substance abuse treatment facilities of the likelihood of this interaction. The clinical effect is usually seen after 7 days of coadministration and may be managed by increasing the methadone dosage, usually in 5-mg to10-mg increments daily until the desired effect is achieved.

Buprenorphine and ART. Buprenorphine, a patial μ-opioid agonist, is administrated sublingually and is often coformulated with naloxone. It is being increasingly used for opioid dependence treatment. The lower risk of respiratory depression and overdose compared with methadone allows it to be prescribed by physicians in primary care for the treatment of opioid dependency. This flexible treatment setting could be of significant value to opioid-addicted HIV-infected patients who require ART because it enables one physician or program to provide both medical and substance abuse services. Limited information is currently available about interactions between buprenorphine and antiretroviral agents [13-14]. Findings from available studies show a more favorable drug interaction profile than that of methadone.

Naltrexone and ART. A once monthly extended-release intramuscular formulation of naltrexone was recently approved for prevention of relapse in patients who have undergone an opioid detoxification program. Naltrexone is also indicated for treatment of alcohol dependency. Naltrexone is not metabolised via the CYP 450 enzyme system and is not expected to interact with protease inhibitors (PIs) or nonnucleoside reverse transcriptase inhibitors (NNRTIs) *[15]*.

Table 11 provides the currently available pharmacokinetic interaction data that clinicians can use as a guide for managing patients receiving ART and methadone or buprenorphine. Particular attention is needed concerning communication between HIV care providers and drug treatment programs regarding additive drug toxicities and drug interactions resulting in opiate withdrawal or excess.

Methylenedioxymethamphetamine (MDMA), GHB, ketamine, and methamphetamine all have the potential to interact with ARV agents because all are metabolised, at least in part, by the CYP 450 system. Overdoses secondary to interactions between the party drugs (i.e., MDMA or GHB) and PI-based ART have been reported *[16]*.

Summary

It is usually possible over time to support most active drug users such that acceptable adherence levels with ARV agents can be achieved *[17-18]*. Providers must work to combine all available resources to stabilize an active drug user in preparation for ART. This should include identification of concurrent medical and psychiatric illnesses, drug treatment, needle and syringe exchange, reduction in high-risk sexual behavior, and harm reduction strategies. A history of drug use alone is insufficient reason to withhold ART because individuals with a history of prior drug use have adherence rates similar to individuals who do not abuse drugs. Important considerations in the selection of successful regimens and the provision of appropriate patient monitoring in this population include supportive clinical sites; linkage to substance abuse treatment; and awareness of the interactions between illicit drugs and ARV agents, including the increased risk of side effects and toxicities. Simple regimens should be considered to enhance medication adherence. Preference should be given to ARV agents that have a lower risk of hepatic and neuropsychiatric side effects, simple dosing schedules, and minimal interaction with methadone.

Table 11. Drug interactions between antiretroviral agents and drugs used to treat opioid addiction

Concomitant Drug	Antiretroviral Class/Drug	Pharmacokinetic Interactions Recommendations/Clinical Comments
Buprenorphine	EFV	buprenorphine AUC ↓ 50%; norbuprenorphine* AUC ↓ 71% No withdrawal symptoms reported. No dosage adjustment recommended; however, monitor for withdrawal symptoms.
	ATV	buprenorphine AUC ↑ 93%; norbuprenorphine AUC ↑ 76%; ↓ ATV levels possible. Do not coadminister buprenorphine with unboosted ATV.
	ATV/r	buprenorphine AUC ↑ 66%; norbuprenorphine AUC ↑ 105% Monitor for sedation. Buprenorphine dose reduction may be necessary.
	DRV/r	buprenorphine: no significant effect, norbuprenorphine AUC ↑ 46% and Cmin ↑ 71%. No dose adjustment necessary.
	TPV/r	buprenorphine: no significant effect; norbuprenorphine AUC, Cmax, and Cmin ↓ 80% TPV Cmin ↓ 19%–40%. Consider monitoring TPV level.
	3TC, ddI, TDF, ZDV, NVP, LPV/r, NFV	No significant effect No dosage adjustment necessary.
	ABC, d4T, FTC, ETR, FPV +/- RTV, IDV +/- RTV, SQV/r, RAL, MVC, T20	No data
Methadone	ABC	methadone clearance ↑ 22%. No dosage adjustment necessary.
	d4T	d4T AUC ↓ 23% and Cmax ↓ 44%. No dosage adjustment necessary.
	ZDV	ZDV AUC ↑ 29%–43%. Monitor for ZDV-related adverse effects.
	EFV	methadone AUC ↓ 52% Opioid withdrawal common; increased methadone dose often necessary.
	NVP	methadone AUC ↓ 41%. NVP: no significant effect Opioid withdrawal common; increased methadone dose often necessary.
	ATV/r, DRV/r, FPV/r, IDV/r, LPV/r, SQV/r, TPV/r	With ATV/r, DRV/r, FPV/r: R-methadone† AUC ↓ 16%-18%; With LPV/r: methadone AUC ↓ 26%–53%; With SQV/r 1,000/100mg BID: R-methadone AUC ↓ 19%; With TPV/r: R-methadone AUC ↓ 48% Opioid withdrawal unlikely but may occur. No adjustment in methadone usually required; however, monitor for opioid withdrawal and increase methadone dose as clinically indicated.
	FPV	No data with FPV (unboosted) With APV: R-methadone Cmin ↓ 21%, AUC no significant change Monitor and titrate methadone as clinically indicated. The interaction with FPV is presumed to be similar.
	NFV	methadone AUC ↓ 40% Opioid withdrawal rarely occurs. Monitor and titrate dose as clinically indicated. May require increased methadone dose.
	ddI (EC capsule), 3TC, TDF, ETR, RTV, ATV, IDV, RAL	No significant effect No dosage adjustment necessary.
	FTC, MVC, T20	No data

*Norbuprenorphine is an active metabolite of buprenorphine. † R-methadone is the active form of methadone.

Acronyms:

3TC = lamivudine, d4T = stavudine, ddI = didanosine, APV = amprenavir, FPV = fosamprenavir, FPV/r = fosamprenavir/ritonavir, ABC = abacavir, AZT = zidovudine, RTV = ritonavir, NFV = nelfinavir, ATV = atazanavir, ATV/r = atazanavir/ritonavair, FTC = emtricitabine, TDF = tenofovir, RAL = raltegravir, IDV = indinavir, IDV/r = indinavir/ritonavir, LPV/r = lopinavir/ritonavir, NVP = nevirapine, EFV = efavirenz, ETR = etravirine, TPV = tipranavir, PV/r = tipranavir/ritonavir DRV/r = darunavir/ritonavir, MVC = maraviroc, T20 = enfuvirtide, SQV/r = sacquinavir/ritonavir.

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CONFERENCE REPORTS

European Association of the Study of the Liver Monothematic Conference on Hepatitis D

24-26 September 2010, Istanbul, Turkey

Needs of neglected disease going unmet: a conference overview

Anastasiya Solovyeva, ITPCru

A specialised conference on hepatitis Delta (D) took place on 25-26 September 2010, in Istanbul, Turkey. The conference was organised by the European Association for the Study of the Liver (EASL) and gathered together almost 200 health professionals.

This was the first conference on hepatitis D and for the first time the available information about the D virus was presented. Many aspects of Hepatitis D were highlighted: virology, pathogenesis, epidemiology, diagnosis and natural history, treatment, prevention and future development.

In 1977, Mario Rizzetto and colleagues described a novel antigen in the nucleus of hepatocytes derived from patients infected with HBV. Antibodies against the so-called 'delta antigen' were detected in patients with a particularly severe course of HBV infection. Subsequently, the hepatitis D virus (HDV) was identified as the infectious agent causing hepatitis in the presence of HBV infection. Thus, hepatitis D can occur only in individuals who are also infected with HBV, as HDV uses the hepatitis B surface antigen (HBsAg) as its envelope protein, which is essential for viral transmission. HDV infection can therefore occur as either a superinfection of chronic HBV infection or as simultaneous acute HBV and HDV coinfection.

Chronic HDV is by far the most dangerous hepatitis virus. It leads to more severe disease than hepatitis B mono-infection and more rapid rates of fibrosis progression. In HDV there is a relatively early decompensation. Hepatitis D patients are in a greater risk of developing a hepatocellular carcinoma. There are currently no established treatment options. Limited data suggest that hepatitis D is mainly an immune-mediated disease, at least in patients with HDV genotypes 1 and 2. Antiviral therapies should, therefore, aim to enhance anti-HDV immunity and reduce viraemia to confer long-term control of infection.

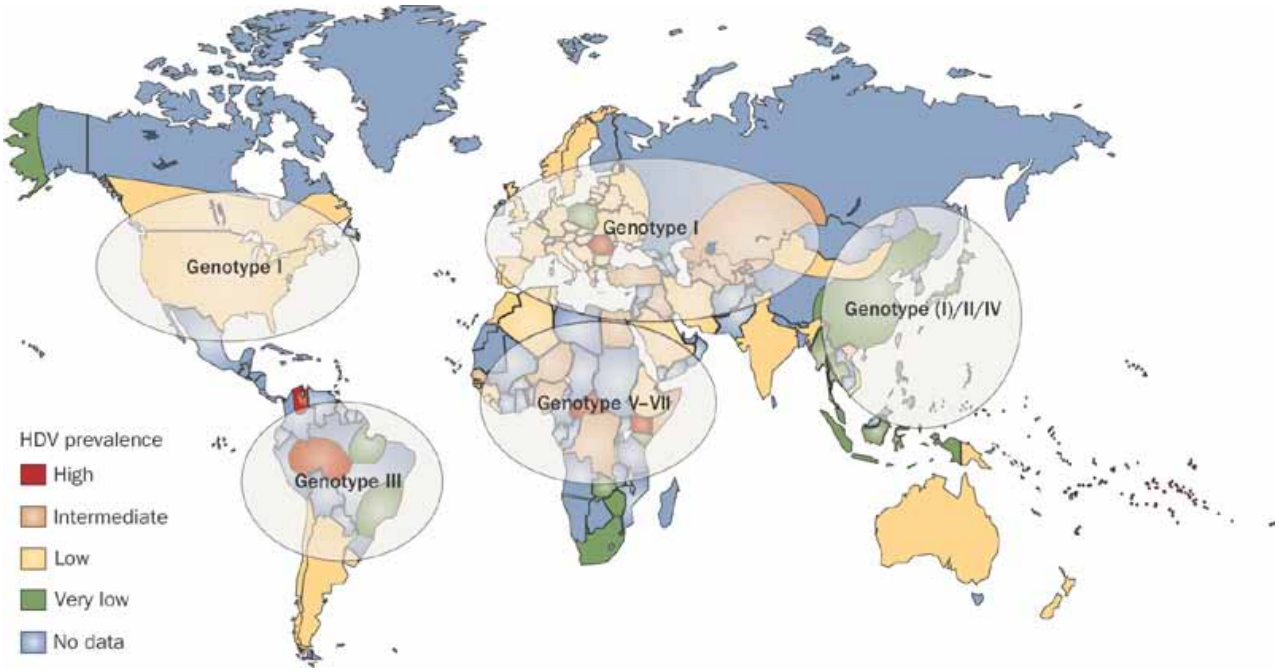
Comprehensive data on epidemiology of hepatitis D are missing. Nevertheless, 15–20 million people are estimated to have HDV globally. Other sources estimate 20-50 million people. However, this may still be an underestimation since epidemiology data from

many areas where hepatitis B is highly prevalent are missing. Epidemiology of HDV is changing. In Europe, comprehensive data is available: 8—12% HBsAg positive patients were tested anti-HDV positive, most of the European HDV patients were born in highly endemic areas like Eastern Turkey, Eastern Europe, Central Asia, Africa, Southern America, Western Pacific. There is an urgent need for reliable data especially from highly endemic regions.

Even 30 years after discovery of HDV, its life cycle is not fully understood. The virus enters the hepatocyte via unknown receptor. The entry mechanisms of HBV and HDV are not fully described, but they are a therapeutic target for future antiviral drugs. Prenylation inhibitors are about to enter humans studies.

HDV has a great genetic variability. There are 8 genotypes and possibly several subclades, according to a French research by Emmanuel Gordien, who used 1116 samples for phylogenetic analysis collected between January 2001 and December 2009.The research showed that the distribution of clades is global.

Fig 1. Global epidemiology of HDV infection according to viral genotype



Source: Wedemeyer H and Manns MP. Epidemiology, pathogenesis and management of hepatitis D: update and challenges ahead. Nat. Rev. Gastroenterol. Hepatol. (2010). doi:10.1038/nrgastro.2009.205.

Every individual who is HBsAg positive should be tested for anti-HDV IgG antibodies at least once. There is no evidence that direct testing for HDV RNA in the absence of anti-HDV antibodies is of any use because anti-HDV antibodies develop in every individual infected with HDV. A positive result for the presence of anti-HDV antibodies, however, does not necessarily indicate active hepatitis D; HDV RNA can disappear indicating recovery from HDV infection. In the long term, anti-HDV antibodies can disappear after recovery from infection. However, anti-HDV antibodies may persist for years, even when following HBsAg seroconversion or liver transplantation.

HDV infection should be confirmed by the detection of serum HDV RNA. If an individual tests positive for serum HDV RNA, subsequent evaluation including grading and staging of liver disease, surveillance for hepatocellular carcinoma and consideration for antiviral treatment is indicated. HDV RNA quantification is offered by some laboratories. However, similar to HCV, there is no evidence that serum HDV RNA levels correlate with any clinical marker of activity or stage of liver disease. Thus, HDV RNA quantification is only useful if antiviral treatment is indicated. Rules regarding the discontinuation of antiviral treatment depending on the level of HDV RNA decline are under evaluation.

Erhardt *et al.* have suggested that patients with less than a three log decline in serum HDV RNA levels after 24 weeks of treatment with PEG-IFN-alpha2b do not benefit from continued treatment. Similarly, Yurdaydin *et al.* showed that patients with HDV infection who achieve an SVR with conventional recombinant IFN-alpha usually show a decline in serum HDV RNA levels within the first 3–6 months of treatment compared with patients who are not able to clear HDV infection.

Prophylaxis against HDV is HBV vaccination and there remains a need for an HDV specific vaccine to protect HBsAg carriers in endemic areas or risk populations.

Coinfection with HDV and HIV is associated with higher replication markers of HDV and accelerated liver fibrosis progression. HIV-associated immunodeficiency favors viral replication escape, abrogating viral interference phenomena of hepatitis viruses. All viruses B, C and D may replicate in a given patient. Since the introduction of HAART in 1996, most HIV-positive people

have experienced immune recovery and severe immunodeficiency is currently rare. The worst prognosis of viral hepatitis in this population has ameliorated in recent years. The wide use of oral antivirals with dual activity against HIV and HBV (tenofovir, 3TC, FTC), alone or in combination, provides a unique opportunity to explore their long-term effect on HDV in co-infected patients. (Soriano et al. AIDS 2005).

In the summary of his talk about EuroSIDA, Vincent Soriano said that the prevalence of anti-HDV in chronic HBsAg carriers in EuroSIDA is 12%. Up to 85% of these patients show HDV viremia. Overall patients with delta hepatitis show lower serum HBV-DNA levels than HBsAg+ carriers without delta hepatitis. However, in the subset of delta hepatitis patients with HBV-D, less inhibition of HBV replication was found. (Soriano et al, 2009).

The incidence and prevalence of delta hepatitis and HDV-related liver disease in the HIV population has dramatically declined since year 2006: HAART, broad HBV vaccination, decline in IDU, closer medical follow-up, no alcohol behavior, early diagnosis, proper follow-up of cirrhosis and other measures played its positive role.

HIV associated immunodeficiency is believed to be associated with a worsening in the natural history of chronic HDV, with evidence of increased replication markers (HDV-RNA levels and frequency of serum delta antigen recognition) and faster progression to the end stage liver disease. Early introduction of antiretroviral therapy might minimise these deleterious effects, by suppressing HIV replication and enhancing immune responses. Moreover, the use of potent anti-HBV agents with antiretroviral activity, such as tenofovir, has been associated with a steadily significant decline in serum HDV-RNA and amelioration of liver disease in a subset of HIV-positive patients with HDV, an observation, which requires further investigation (Sheldon et al, 2008). More recently, a small subset of HIV-HBV-HDV co-infected patients on long-term tenofovir/FTC therapy evolved to serum HBsAg clearance, which in all instances was preceded by a steadily decline in serum HBsAg titers. Serum HDV-RNA also became undetectable in these individuals. The question is whether the a cure for delta using nucleos(t)ide analogues was obtained.

Exposure to HCV preceding or following acquisition of HDV results in viral interference, which in most instances leads to replication of one virus and suppression of the other (Martin-Carbonero et al, 2007). It is HDV, which in most cases suppress HCV, which in general results in sustained clearance of HCV. In a subset of patients, however, and particularly in the presence of immunosupression (i.e. in HIV co-infection with low CD4 counts), replication of all viruses (HBV, HDV, HCV) may be recognised at all times points intermittently (Schaper et al, 2010).

Although treatment with pegylated interferon plus ribavirin may clear HCV in some of these triply or quadriply infected patients viremic for HCV, no sustained benefit is generally seen for hepatitis D following treatment discontinuation (Soriano et al, 2007).

The major challenges for hepatitis D are that it is a defective virus, its replication circle is unconventional and it is highly pathogenic (HDV causes the least common, but most severe form of chronic viral hepatitis, leading to cirrhosis in about 50-70% of the cases).

Despite been rare, because of the lack of an effective treatment and the severity of liver disease, chronic HDV is a serious health problem. Because of the paucity of the patients, most of the studies related to chronic HDV are inconclusive. Interferons and pegylated interferons may provide a 15 to 45% sustained virologic response. The replication strategy of delta virus is different from that of hepatitis B virus. Therefore, the nucleos(t)ide analoges, which are effectively used in the treatment of chronic hepatitis B, have no place in the treatment of CHD. These drugs may be beneficial only if they success a reduction in the level of HBsAg, which is required for the formation of the delta virion.

Lamivudine (3TC), which is commonly used to treat HBV (despite the risk of resistance), does not decrease the level of cccDNA or HBsAg. Therefore, it has no effect in the treatment of chronic HDV, either as a monotherapy or as a part of interferon combination. In a randomised study, improvement in necroinflammatory activity was found to be more significant in the combination group, comparing to interferon-treated patients. However, no significant improvement was observed in regards to fibrosis. The rate of sustained virologic response was statistically similar in combination therapy and interferon treated patients.

In recent years the most powerful antivirals have been shown to decrease the HBsAg titer and to achieve HBsAg loss. Some promising results are expected from the combination therapies of interferon with entecavir or tenofovir disoproxil fumarate (TDF). A case report described an HBsAg seroconversion after 10 month treatment of peginterferon alfa-2a plus TDF plus emtricitabine (FTC). Although there are ongoing studies investigating the effectiveness of interferons, tenofovir and entecavir in HDV, there has been no published clinical study so far.

Based on the data of the reducing effect of adefovir dipivoxil on cccDNA and HBsAg titer, its combination with peginterferon alpha-2a was investigated (Wedemeyer et al, 2006). This study demonstrated no difference between peginterferon alpha-2a (PegIFN2a) and PegIFN2a+adefovir combination, in terms of HDV RNA negativity. However, HBsAg reduction was more pronounced in combination arm comparing to monotherapies. 40% of the patients in the combination arm achieved at least 1 log reduction of HBsAg level, while this figure is 5% in the PegIFN 2a-treated patients.

Ribavirin is effective against hepatitis C virus, and it has been shown experimentally to inhibit HDV genome replication in hepatocyte cultures. However, in a pilot study, including patients with chronic HDV, ribavirin monotherapy did not result in biochemical, virological or histologyical improvements (Garripoli A et al, 1994). Yet, ribavirin was tried in a combination with interferons in the treatment of CHD. In these trials, ribavirin combinations were not superior to interferon monotherapy. Two years duration of interferon plus ribavirin treatments (Kaymakoglu S et al, 2005; Gunzar F et al, 2005) and a 24-week peginterferon plus ribavirin combination (Niro G et al, 2006) achieved almost 20% sustained virologic response in patients with chronic HDV. Interferon and nucleos(t)ide combination therapies do not provide an additive or synergistic effect in the treatment of HDV. “However, the combinations with newer drugs are awaited with interest”, - said Doctor Akarca from Ege University Medical School, Izmir, Turkey.

Currently, the only option for treating HDV is IFN-a or pegIFN-alpha, resulting in moderate sustained virological response rates at long term and high dose application. Experimentally it has been shown that inhibitors of farnesyltransferase inhibit HDV secretion in mice by blocking farnesylation of the large HDAg. Some other specific approaches like the inhibition of the HDV-ribozyme or siRNA are feasible but far from entering the clinical stages. Thus there is a strong medical need to develop drugs that interfere with specific stages of HDV replication.

In a summary at the end of the conference, Dr Manns emphasised that there are many needs that concern us: improved awareness (Anti HDV in every HBsAg+ patient, standardised HDV RNA testing, increased funding for basic science, convincing governments to invest in research for HDV), promoting the importance of HDV infection to governments, foundations (Gates), EASL, AASLD, diagnostic companies, therapeutic companies. He also suggested the creation of International HDV Consortium (without formal membership, driven by projects, working on global database, collection of material (serum, DNA, tissue), and leading the interventional clinical trials).

CONFERENCE REPORTS

18th International AIDS Conference

18-23 July 2010, Vienna, Austria

Introduction

Treatment access will always dominate the programme of World AIDS Conferences. Since the Durban conference in 2000, every scientific advance at this meeting is rightly seen in the context of which populations, in a global health emergency, will have the opportunity to benefit.

This is one of the strengths of this meeting, which now has over 20,000 delegates, and many of the access-related sessions are online as webcasts and transcripts produced by the Kaiser Foundation.

A joint report from UNAIDS and Kaiser launched prior to the conference clearly and disturbingly showed that international donor funding, which now supports close to five million people on treatment, has leveled. This threatens to overturn the accumulated health benefits from the last ten years. Flat-lined funding means treatment programmes will be closed to new patients and this will have a disastrous impact on HIV prevention.

Without treatment, not only is there little incentive to test, and an increase in AIDS and death, but also the beneficial impact that antiretroviral therapy has on the risk of transmission will be reduced. And treatment is still likely to be more effective in preventing HIV than any other intervention.

This global crisis demands international support, and this involves funding. So while the US leads funding initiative, as the world's richest country, it is just as important that other wealthy nations meet, for example, the commitments made at the G8 summit. The expense and investment in the conference itself, did not sit easily with the decision to hold the meeting in country that has not supported the Global Fund since 2002. Currently the Global Fund to Fight AIDS, TB and Malaria (GFATM) is faced with a $3 billion shortfall for 2010. Similarly, very few African nations have met their pledge in the Abuja Declaration 2001 to target at least 15% of GDP on healthcare.

The global demand for treatment challenges the concept of universal access using todays medications. Research into ARV drug delivery using nanotechnology is proceeding extremely slowly with only one abstract at this meeting, and yet this has the potential to address many obstacles to wider access. The volume of active ingredient is dramatically reduced with a nanoformulation requiring perhaps monthly dosing, both of which dramatical reduce costs.

This was a conference that highlighted access issues from a human rights perspective:

- The Vienna Declaration - is the official conference statement seeking to improve community health and safety by calling for the incorporation of scientific evidence into illicit drug policies (viennadeclaration.com).
- Many sessions addressed access to evidence-based harm reduction stategies including opioid substitution therapy (OST) and needle exchange progammes.
- Access to treatment to prevent mother-to-child transmission (PMTCT) – currently only 10–20% of HIV-positive women worldwide are able to access testing and treatment during pregnancy.
- The criminalisation of same sex relationships and discrimination against men and women whose sleep with partners of the same sex, highlighted most recently by extreme cases in Uganda, Malawi and Iran, was the focus of several sessions. .

In terms of medical and scientific research, there were a few important headline-grabbing studies and a good selection of interesting but preliminary research findings.

As with all meeting reports we include links to original abstracts and webcasts when available, and for this meeting we also start with a guide on how to navigate the conference website for other material.

Abstracts from the conference are published on the conference website:

http://www.aids2010.org/

Navigating the conference online

Simon Collins, HIV i-Base

As with previous IAS conferences, much of the conference material is available online and reports in ARV4IDUs include appropriate hyperlinks.

Locating the appropriate files, presentations, webcasts, transcriptions or even the basic abstracts is more challenging. Access is routed through the 'Programme at a glance' link on the conference homepage. This requires a free software plug-in called Silverlight, but an automatic download button should come up if you do not already have this installed.

The search facility requires selecting one of the seven options directly under the search bar ie to search the abstracts, you need to first click 'abstract' which when selected has the tiny white triangle in the red block turn to face down. Then search as you would normally by entering a keyword in the search box and clicking search. Results come up listed below.

The abstract books are available to download as free PDF files, but only for each day, so searching the whole conference requires repeating each search four times.

Although you can browse sessions by day and time, this is not so easy if you are looking for a specific session but don't know when it was presented because there is not a programme that just shows the sessions. For example a search for 'late breaker' brings up no results whether searching 'programme at a glance', 'abstracts', or 'oral sessions'.

If you find a session page, you then have to find and click the yellow 'more info' button at the bottom right of an empty box, and then you finally get to a page that makes sense. Don't be entirely fooled. The 'abstract' links seems to work, but 'slides with audio' are not always available and the 'powerpoint' link doesn't work at all. For presentation slides, scroll further down the page where slides that are available are listed under the 'powerpoint presentations' heading.

The audio works but you need to manually download the powerpoint slides to really follow the presentation.

To make things more confusing, some webcast presentations are provided by Kaiser Foundation on a different website.

http://globalhealth.kff.org/AIDS2010

These webcasts only show the presenter, with no slides and no easy links to slides. Although you often hear two different presentations simultaneously, this accurately captures the conference experience. Only a cloth curtain divided most session rooms, so the webcasts accurately reflect the conference atmosphere, including this difficulty.

Kaiser provide rough transcripts of the sessions that can be more useful with the slide set, than the webcast, though they are draft transcripts only.

Web access should be a leading priority for these conferences. The interface used by the Retrovirus (CROI) conference would be a much more useful model to use and would make this aspect of the meeting far more accessible, whether provided by IAS or Kaiser.

The Lancet series: Global HIV epidemic among people who use drugs

Svilen Konov, HIV i-Base

Even though majot HIV treatment conferences hardly cover IDU issues and the big news is that there is no news, the 18th International AIDS Conference proved me wrong.

The symposium, organised by *The Lancet* and entitled Global HIV epidemic among people who use drugs, was perhaps the single most important event tackling the topic during the last five or more years.

This session included seven state-of-the-art reviews, and a number of invited commentaries, all of which were published as a supplement to the Lancet, and which are free to access online (after intial free registration).

"Following the principle of "nothing about us without us," each paper included the voices of people who use drugs. These include community participants and leaders from China, Ukraine, Thailand, Malaysia, and the USA. Invited commentaries include the Vienna Declaration, a call to decriminalise people who use drugs, and commentaries from high profile authors including state officials from Mexico who will discuss their country's alternative approaches to the war on drugs, and commentaries on women and drug use, alcohol and HIV transmission in Africa. The series captures a 'sea change' in terms of the international response to HIV prevention and treatment among people who use drugs, a growing segment of the global HIV and AIDS epidemic that has

been underappreciated for too long".

All documents from the symposium are posted online.

http://pag.aids2010.org/session.aspx?s=155

These include all presentation slides and audio recording (including in Russian), as well as all PowerPoint presentations for download. Further to that, the Kaiser Family Foundation provides webcasts both in English and Russian, including transcripts of the talks.

http://globalhealth.kff.org/AIDS2010/July-20/The-Lancet-Series.aspx

Articles in *The Lancet* are also online. The site requires registration, but it is free for this particular issue.

http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(10)60832-X/abstract

We recommend readers to view this symposium online, summaries are included below for some sessions.

Steffanie Strathdee from the University of California, San Diego, presented HIV and the risk environment among people who inject drugs: past, present, and projections for the future. [1]

The team systematically reviewed reports about determinants of HIV infection in injecting drug users from 2000 to 2009 and then modelled changes in risk environments in regions with severe HIV epidemics associated with IDU. The model clearly showed a heterogeneity in the number of HIV infections resulted from IDU and unprotected sexual intercourse. The estimations for 2010-2015 suggest that HIV prevalence can be reduced by 41% in Odessa (Ukraine), 43% in Karachi (Pakistan), and 30% in Nairobi (Kenya) through a 60% reduction of the unmet need of programmes for opioid substitution, needle exchange and provision of ARV.

The next presentation by Louisa Degenhardt was entitled HIV prevention for people who inject drugs: why individual, structural, and combination approaches are required. [2]

The researchers summarised evidence on the effectiveness of individual level approaches to prevention of HIV-infection, ie opioid substitution therapy, needle and syringe exchange programmes and ARV provision and afterwards modelled the effect of increased coverage and combination of the three approaches. The model shows that each intervention take individually will provide only modest reductions in HIV transmission, hence it is suggested that prevention needs high coverage and combined approaches. Some possible social and structural changes were also discussed.

Next three presentations were particularly topical . The first of those was by Daniel Wolfe on Treatment and care HIV-infected people who inject drugs: a review of barriers and ways forward. [3]

This presentation was based on a review of evidence for effectiveness, cost-effectiveness, and coverage of ARV for IDUs with a particular stress on low- and middle-income countries. Almost half of the IDUs living with HIV (47%) are concentrated in five countries-China, Russia, Ukraine, Vietnam and Malaysia. IDUs are 67% of the cumulative HIV cases in those countries, but only 25% of them receive ARV. For improvement of this situation, the writers suggest systemic and structural changes like integration of ARV provision with opioid substitution and TB treatment, increased peer engagement in treatment delivery and reform of harmful policies, ie. police use of drug user registries, detention of drug users, imprisonment for possession of drugs for personal use, etc.

Frederick Altice's talk was entitled Medical, psychiatric and substance use co-morbidities among HIV-infected drug users: optimizing treatment and clinical outcomes. [4]

The presentation is of particular value, as it recognised that simultaneous clinical management of multiple comorbidities, that are more typical for HIV-positive IDUs than for the general HIV-positive population, might result in complex pharmacokinetic drug interactions that must be addressed accordingly. The article in *The Lancet* has several tables that will help medical professionals and treatment peer counsellors. Those tables present information on:

- Common legal and illegal drugs and their effect on HIV;
- Available pharmacological medication-assisted therapies used for treatment of substance-use disorders;
- Complications related to drug use in HIV-infected IDUs; and
- Common interactions between methadone and buprenorphine with treatment for HIV infection and other comorbidities.

The next presentation was on Amphetamine-group substances and HIV: what is to be done? by Grant Colfax. [5]

As amphetamine-group substances are used worldwide and are more prevalent than either cocaine or opioids, the researchers did a meta-analysis of randomized controlled studies of behavioural interventions for their use. 13 studies with a cumulative sample size of 1997 subjects met the inclusion criteria of the analysis. Overall, high intensity behavioural interventions were moderately effective. The researchers concluded that they: "Did not find conclusive evidence that behavioural interventions as a group are more effective than are passive or minimum treatment for reduction of amphetamine-group substance use or sexual risk behaviours."

The topic of 'People who use drugs, HIV, and human rights' was also touched upon during the talk by Ralf Jurgens. [6]

He presented reports that clearly demonstrate a link between human rights abuses and vulnerability to HIV. These abuses include denial of harm reduction services, discriminatory access to ARV, abusive law enforcement practices, and coercion in the guise of treatment for drug dependence.

Finally, to set the scene for the general discussion that was particularly lively, there was a closing presentation by Chris Beyrer on 'Galvanising a global response: a call to action for HIV and AIDS among people who use drugs'. [7]

According to the team of writers and based on the published work on HIV and in IDUs, the global burden of HIV infection in this group can be reduced. The researchers identified synergies between biomedical science, public health, and human rights. Currently, only about 10% of the IDUs worldwide are reached with necessary services, hence the appalling state of HIV infection spread among the group. To change this situation will take commitment, advocacy, and political courage.

References:

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http://pag.aids2010.org/flash/?pid=100315
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http://pag.aids2010.org/flash/?pid=100314
3. Wolfe D et al. Treatment and care HIV-infected people who inject drugs: a review of barriers and ways forward 18th International AIDS Conference. 18-23 July, 2010. Vienna. Symposium presentation TUSY0704
http://pag.aids2010.org/flash/?pid=100315
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http://pag.aids2010.org/flash/?pid=100312
5. Colfax G et al. Amphetamine-group substances and HIV: what is to be done? 18th International AIDS Conference. 18-23 July, 2010. Vienna. Symposium presentation TUSY0706
http://pag.aids2010.org/flash/?pid=100311
6. Jurgens R et al. The topic of People who use drugs, HIV, and human rights. 18th International AIDS Conference. 18-23 July, 2010. Vienna. Symposium presentation TUSY0707
http://pag.aids2010.org/flash/?pid=100310
7. Beyrer C et al. Galvanizing a global response: a call to action for HIV and AIDS among people who use drugs.18th International AIDS Conference. 18-23 July, 2010. Vienna. Symposium presentation TUSY0708
http://pag.aids2010.org/flash/?pid=100309

HTLV-II molecular epidemiology from HIV-1 infected Spanish injecting drug users

Svilen Konov, HIV i-Base

The Human T-lymphotropic virus-II (HTLV) is a human RNA retrovirus. It shares approximately 70% genomic homology (structural similarity) with HTLV-I. Unlike HTLV-I, HTLV-II has not been clearly linked to any disease, but has been associated with several cases of myelopathy and tropical spastic paraparesis. HTLV-II infection has been predominantly detected in intravenous drug users (IDU) in urban areas of North America and some European countries, who often are coinfected with HIV-1. Subtype HTLV-IIa is the main circulating subtype in North America and Northern Europe while subtype HTLV-IIb is found in Southern Europe, especially in Italy and Spain.

Abad and colleagues looked into the epidemiology of the HTLV-II in Spain. They included 12 HTLV-II positive IDUs from Spain, coinfected with HIV-1 in the study. The researchers used proviral DNA extracted from participants' peripheral blood mononuclear cells. The samples were sent for PCR. Amplified fragments from all Long terminal repeat (LTR) (389 bp),*env* (777 bp) and *tax* (993bp) regions were sequenced. The sequences were compared with HTLV-IIa prototype (Mo) and HTLV-IIb prototypes (G12 and NRA). Phylogenetic analysis was carried out together with reported sequences of all HTLV-II subtypes using the STLV-2 as an outgroup. One thousand bootstrap replicates were used to support the tree using the Unweighted Pair Group Method with Arithmetic Mean (UPGMA).

Sequence analysis confirmed that the samples studied belonged to HTLV-II subtype b. The regulatory elements were highly conserved for LTR, as well as functional domains for env and tax proteins.

The researchers concluded that HTLV-IIb remains the most frequent subtype in Spain. Besides, phylogenetic analysis showed that Spanish sequences shared many similarities with Portuguese and Italian ones. All of them obtained from intravenous drug users coinfected with HIV-1.

Ref: Abad M et al. HTLV-II molecular epidemiology from HIV-1 infected Spanish injecting drug users. 18th International AIDS Conference. 18-23 July, 2010. Vienna. Poster abstract CDC0388
http://pag.aids2010.org/Abstracts.aspx?AID=13142

Injecting drug use and ART: monitoring survival on treatment

Svilen Konov, HIV i-Base

Iran has a concentrated HIV epidemic among the IDU sub-population. As a result, a significant number of people who need ART are either IDU or ex-IDU. In some studies it has been demonstrated that IDUs benefit less from ART due to higher mortality or less adherence to treatment.

A team of researchers in Iran conducted a study to look more in-depth onto those previous assertions. In a historical cohort study the records of registered patients on ART were reviewed to determine their survival on treatment and its determinants. Data were gathered back to 2000 for 362 patients in nine provinces. Socio-demographic characteristics, drug use history, being on methadone maintenance treatment (MMT), CD4 count, the date of starting and discontinuation of treatment and its reason were all extracted. Non-adherence and mortality were analysed separately.

The data showed that one-year overall survival on treatment was 82%. Analysing non-adherence, being on MMT, being single or widowed and, and being a woman were factors with statistically significant effect on survival, not limited to the first year. Analysing mortality, current drug use, age (fifty and over) at the time of starting treatment, and lower levels of education were the determinants of a lower survival rate.

The study showed that IDU itself was associated with higher mortality than non-adherence, which is in accordance with other findings supporting the capability of IDUs to follow complex ART regimens; nevertheless, their other drug-related health problems have to be considered as well. On the other hand, MMT was associated with lower survival on ART due to non-adherence suggesting two main issues; possible not following the MMT guidelines completely and/or a possible drug interaction between methadone and ART, resulting in a lower methadone blood concentrations.

Ref: Taj M et al, Injecting drug use and ART: monitoring survival on treatment. 18th International AIDS Conference. 18-23 July, 2010. Vienna. Poster abstract CDC0945

http://pag.aids2010.org/Abstracts.aspx?AID=5831

Dopaminergic signaling: a common neuropathogenic mechanism in the etiology of opiate addiction and neuro-AIDS

Svilen Konov, HIV i-Base

It is hypothesised that the modulation of the dopaminergic pathway may underlie the exacerbation of HIV encephalopathy observed with opiate abuse. An important constituent of dopaminergic activities within the brain is a 32 kDa dopamine and adenosine 3´,5´-monophosphate-regulated phosphoprotein (DARPP-32) which is recognised to be critical to the pathogenesis of drug addiction. Genetic polymorphisms within Dopamine Transporter gene (DAT1) are associated with individual differences in DA (Dopamine) functioning that may contribute to varying degrees of neurocognitive impairment.

Mahajan S and colleagues researched whether DARPP-32 signaling pathway is the central molecular mechanism that integrates the neuropathogenic activities of both HIV-1 and opiate abuse and that examining DA-related genetic polymorphisms in these patients may provide insight into the susceptibility to and progression of HIV-associated neurocognitive disorders (HAND).

In order to do that, they obtained snap frozen human brain tissue samples (n=8/group) from National NeuroAIDS Tissue Consortium (NNTC) at autopsy from HIV-1 patients who abused/did not use opiates and who had varying degrees of HAND. Using real time QPCR and immunoblotting methods they examined the gene and protein expression levels of DARPP-32; genetic polymorphisms in the DAT1 gene, in the brain tissue samples and correlated the expression levels of these genes to the severity of neurocognitive impairment in these patients.

Data showed a significant increase in the total DARPP-32, Phospho^{thr34} DARPP-32 and DAT1 expression in HIV-1 patients who abused opiates and a significant positive correlation between expression levels of these genes and the severity of HAND.

The conclusion of the researchers was that a combination of HIV-1 and opiate abuse has an adverse impact on the dopaminergic system and contributes to significant neurocognitive impairments in HIV-1 patients who abuse drugs, confirming the role of the dopaminergic pathway in the pathogenesis of HAND.

Ref: Mahajan S et al, Dopaminergic signaling: a common neuropathogenic mechanism in the etiology of opiate addiction and Neuro-AIDS. 18th International AIDS Conference. 18-23 July, 2010. Vienna. Poster abstract CDA0007.

http://pag.aids2010.org/Abstracts.aspx?AID=4170

Characteristics of peripheral blood mononuclear cells of injecting drug users

Svilen Konov, HIV i-Base

Even though cryopreservation is a common practice nowadays, because it allows both functional and phenotypic analyses, it may induce significant changes in the cell viability, in cytokine production and in the surface markers of peripheral blood mononuclear cells (PBMC), which may also alter the efficiency of T cell stimuli. This may be particularly true when the samples are obtained from IDUs, as IDU leads to chronic organism intoxication that causes a system-wide exhaustion and pathological changes of organs. It is unclear then how the PBMC of IDUs will be affected by cryopreservation. Kukhareva P from the Biomedical Centre of St Petersburg (Russian Federation) reported on a project which main goal was to create standard operation procedures for IDUs PBMC isolation, cryopreservation and thawing.

She isolated PBMC by density gradient centrifugation on ficoll-paque and then followed the standard procedures for cryopreservation. For representation of surface markers and intracellular cytokines flow cytometric assay was used. To measure secretion of IFNγ in response to CMV stimulation she usedIntracelularcytokine staining (ICS).

Results clearly indicated that PBMC of IDUs can be stored at a concentration of 2,5 million/ml up to a month without a significant reduction in survival and number. Blood of drug users can be stored up to 7 hours before the isolation of the PBMC. Isolation on fikoll gradient and cryopreservation affect the composition of certain subpopulations of the PBMC of IDUs and healthy donors. Defrosted PBMC samples ofIDUs are suitable for assessing immune response with specific and nonspecific activation, therefore IDU does not affect the immunological characteristics of the PBMC in fresh and cryopreserved samples.

Ref: Kukhareva P, Characteristics of peripheral blood mononuclear cells of injecting drug users. 18th International AIDS Conference. 18-23 July, 2010. Vienna. Poster abstract CDB0062.

http://pag.aids2010.org/Abstracts.aspx?AID=12466

High frequency of methicillin-resistant staphylococci detection at post-injecting pyo-inflammatory complications in HIV-infected injecting drug users

Svilen Konov, HIV i-Base

Studies have already demonstrated the possibility of post-injection pyoinflammatory complications (PIPIC) in HIV-infected IDUs consuming artificial drugs [1]. The most common complication registered is Staphylococci, however their methicillin-resistance has not been evaluated previously. To determine the role of MRS in various forms PIPIC, Popov A and colleagues carried out an antibiotic sensitivity testing in isolated strains of microorganisms.

The analysis of purulent specimens were studied according to standard bacteriological procedures. Susceptibility to antimicrobial agents was tested with the disk-diffusion method.

The study included 41 subjects (24 male and 17 female; age range 18-31). All of them were IDUs and had HIV-1-infection diagnosis in CDC II stage. Prevailing forms of PIPIC were abscesses (n = 33) and phlegmones (n = 8). 18 cultures of methicillin-resistant staphylococci were isolated. It included 14 cultures of methicillin-resistant S. aureus (MRSA) and 4 isolates of methicillin-resistant S. epidermidis (MRSE). All isolates of MRSA and MRSE retained sensitivity to vancomycin and linezolid.

The data obtained coincide with the general trend of the epidemic spread of MRSA and MRSE in out-of-hospital environment in immunocompetent persons. Empirical antibacterial therapy of PIPIC in HIV-infected IDUs should take into account the high frequency of MRSA and MRSE. This fact must provide a compulsory inclusion of glycopeptide or oxazolidinone antibiotics into the scheme of ethiotropic treatment.

Ref: Popov A, High frequency of methicillin-resistant staphylococci detection at post-injecting pyo-inflammatory complications in HIV-infected injecting drug users. 18th International AIDS Conference. 18-23 July, 2010. Vienna. Poster abstract CDB0091.

http://pag.aids2010.org/Abstracts.aspx?AID=4968

Poorer antiretroviral therapy outcomes in HIV infected injecting drug users in Vietnam

Svilen Konov, HIV i-Base

Of the 35,000 people who have received ART in Vietnam, more than half are current or former IDU. In the IDU subpopulation in the country, the prevalence of HIV-infection can reach up to 60% in certain areas. This situation requires a more in-depth understanding of the differences between IDU and non-IDU patients in treatment response, mortality and loss-to-follow-up.

Le and colleagues used the records of patients attending three adult clinics in provinces with high prevalence from August-September 2008. They included records of people who had started ART at least 6 months prior to that time point. Data were collected on reported drug use, gender, clinical stage, CD4 count, co-infection with viral hepatitis, TB, retention, and survival probability.

Of 1423 eligible people on ART, 1012 (71%) had recorded risk behaviors. Of these, 546 (54%) were IDU. Compared to non-IDU, IDU were more likely ($p < .05$) to be male (95% vs. 44%), coinfected with hepatitis B (16% vs. 12%) or hepatitis C (48% vs. 16%), in WHO clinical stage 3 or 4 (67% vs. 56%) and on TB treatment at ART initiation (15% vs. 6.7%). Median CD4 was significantly lower in IDU at baseline (75 cells/ml vs. 95), and at 6 (176 vs. 209) and 12 (217 vs. 250) months. Median increase in CD4 from baseline was lower in IDU at 6 (91 vs. 106) and 12 (128 vs.150) months. After a median of 16.5 months of follow up, 103 (19%) IDU died and 30 (5.5%) were lost-to-follow-up, significantly higher than non-IDU (8.6% and 2.2% respectively). Survival probability was lower ($p < 0.05$) in IDU than non-IDU after 6 (0.86 vs. 0.93) and 12 (0.79 vs. 0.91) months.

Based on these data, the researchers concluded that in this cohort immunological response was lower, and mortality and loss to follow up higher, among current and former IDU. Urgent interventions to initiate treatment earlier and improve treatment outcomes for IDU are warranted.

Ref: Le YN et al, Poorer antiretroviral therapy outcomes in HIV infected injecting drug users in Vietnam. 18th International AIDS Conference. 18-23 July, 2010. Vienna. Poster abstract CDB0136

http://pag.aids2010.org/Abstracts.aspx?AID=2416

Crystal methamphetamine injection predicts slower HIV RNA suppression among injection drug users

Svilen Konov, HIV i-Base

Crystal methamphetamine (CM) use presents a significant threat to HIV prevention and treatment strategies. CM has been linked to sexual and parenteral risk behaviours and increased likelihood of HIV seroconversion, as well as poor adherence to antiretroviral therapy. In this study, the researchers examined the impact of CM injection on HIV RNA suppression among a prospective cohort of HIV-positive injection drug users (IDUs) initiating antiretroviral therapy. They used Cox regression to model factors that may affect the HIV RNA suppression, based on data obtained from HIV-positive IDUs who were community recruited into a prospective cohort study.

Between September 1996 and April 2008, 384 (54.2%) antiretroviral-naïve patients initiated HAART; 163 (42.5%) of whom were women. 36 (9.4%) reported CM injection at any time during follow-up. The analysis found CM injection to be negatively associated with viral load suppression (RH = 0.63 [95% CI: 0.40 - 0.98]; $p = 0.039$), even after adjustment for age, baseline CD4 cell count and viral load, heroin injection and cocaine injection.

These data indicate negative health outcomes associated with CM use among HIV-positive individuals. It is speculated that the psychopharmacological effects of CM may undermine antiretroviral treatment adherence.

Ref: Fairbairn N et al, Crystal methamphetamine injection predicts slower HIV RNA suppression among injection drug users. 18th International AIDS Conference. 18-23 July, 2010. Vienna. Oral Abstract Session MOAC04; MOAC0405

http://pag.aids2010.org/Abstracts.aspx?AID=13627

Methadone based integrated care for IDUs in Dnipropetrovsk region of Ukraine

Svilen Konov, HIV i-Base

Injecting drug users comprise about 59% of all HIV positive people officially registered in Ukraine and only 7% of those were receiving ARV in 2009.

An the AIDS centre and two Drug Dependence clinics in Dnipropetrovsk region, the most affected in the country, implemented a comprehensive care model. The services provided on site included: Methadone Maintenance Therapy (MMT), HIV testing, CD4 count, viral load, TB testing; examination and counselling by infectious disease doctor, therapist, cardiologist, reproductive health professional, psychiatrist and also psychosocial support was provided.

The programme is being implemented with the financial support of Olena Franchuk ANTIAIDS Foundation and Elton John AIDS Foundation.

Overall, 428 patients (75% male, average age 35-42 years, average period of drugs use of 20 years) were enrolled since July 2008. The overall retention rate was 70%. 74% of all clients of the programme were HIV-positive. 80% of HIV positive clients received their CD4 test results, of which CD4 was below 350 cells in 58%.

Up to 2010, 50% of those met treatment eligibility criteria and started ARV and 40% were enrolled in preparation process to receive ARV. Undetectable viral loads were achieved in 85% of clients receiving ART after 6 months of treatment.

The results of the comprehensive care model clearly indicated that "integration of methadone maintenance therapy (MMT) and ARV is an important tool to enable access to life saving services for IDUs. Out of three clinical settings involved, the AIDS centre appeared to be better positioned to provide integrated MMT/ART services", concluded the researcher.

Ref: Vlasenko L et al, Methadone based integrated care for IDUs in Dnipropetrovsk region of Ukraine. 18th International AIDS Conference. 18-23 July, 2010. Vienna. Poster Exhibition, D46, WEPE 0537
http://pag.aids2010.org/Abstracts.aspx?AID=14048

Risk factors for depression among intravenous drug users (IDUs) receiving antiretroviral (ARV) treatment in Jakarta and Bali, Indonesia

Svilen Konov, HIV i-Base

Depression is common among IDUs living with HIV and is associated with loss of social relationships, increased likelihood of risky behavior, and low-adherence to ARV treatment. Depression, however, often is considered as an insignificant problem, compared to other conditions that require urgent interventions and as a result of that majority of data on depression come from resource richer settings.

Li Y and colleagues looked into some key factors predicting depression in a resource poorer setting, namely Indonesia.
Using a provider referral method, the team recruited and interviewed 142 IDUs receiving ARVs at three HIV clinics in Jakarta (n = 72) and two in Bali (n = 70). A structured questionnaire was used to collect participants' demographic characteristics, history of drug use, treatment experiences, and social support. Depressive symptoms were measured using a 9-item version of the Center for Epidemiologic Studies Depression Scale (CES-D).
92% of the participants were male, young (median age 30), and high school educated (90%). 33% (47) reported using alcohol frequently and/or at least one illicit substance in the past month, and 28% (40) were on methadone maintenance treatment. CES-D scores indicated that 28% (40) of participants were depressed. Multivariate analysis showed that depression was positively associated with recent substance use (OR: 4.6, p=0.003) and being on methadone (OR: 3.6, p=0.02). Older age (per year OR: 0.89, p=0.03), full-time employment (OR: 0.22, p=0.007), and living with parents (OR: 0.19, p=0.003) appeared to have a protective effect.

Ref: Li Y at al, Risk factors for depression among intravenous drug users (IDUs) receiving antiretroviral (ARV) treatment in Jakarta and Bali, Indonesia. 18th International AIDS Conference. 18-23 July, 2010. Vienna. Poster Exhibition D60, WEPE0720
http://pag.aids2010.org/Abstracts.aspx?AID=11385

Effective strategy to scale-up HIV services among injecting drug users (IDUs) in prisons in Bulgaria

Svilen Konov, HIV i-Base

In Bulgaria, the number of prisoners detained for drug-related crimes and drug use increased up to 10-12% of the total prison population after the 2004 amendment of the Penal Code which criminalised the "single dose" possession.

Since 2006, the Ministry of Health and Ministry of Justice jointly introduced the regular provision of anonymous HIV testing and counseling (T&C), in all 12 prisons and 2 detention centres. HIV T&C is provided by staff of public health institutions and NGOs in combination with HBV, HCV and syphilis testing, condom distribution and information materials. HIV-positive people in the penitentiary system are included in the HIV/AIDS patients monitoring system and receive regular follow-up and ARV treatment if needed. In 2009, out of total 9 270 prison population, anonymous HIV T&C was provided to 4,141 people, of who 805 reported history of injecting drug use (9% of total prison population). 27 HIV positive cases were newly diagnosed in IDUs.

In 2009, educational sessions on HIV/STIs prevention were introduced as additional service for 5 425 prisoners, again provided by the outside service providers.

The researchers concluded: "Introducing a comprehensive package of HIV services in prisons provided by outside service providers is effective in scaling-up access to HIV services and active HIV case finding in prisons, especially among IDUs".

Ref: Varleva T et al, Effective strategy to scale-up HIV services among injecting drug users (IDUs) in prisons in Bulgaria. 18th International AIDS Conference. 18-23 July, 2010. Vienna. Poster abstract C54, WEPE0188
http://pag.aids2010.org/Abstracts.aspx?AID=16208

Predictors of weight gain in a cohort of HIV-positive injection drug users (IDUs) initiating antiretroviral (ARV) therapy in Hanoi, Vietnam

Svilen Konov, HIV i-Base

It is documented that initiation of ARV therapy often leads to overall weight gain, but patterns and predictors of weight change over time have seldom been examined.

Tang A et al recruited 100 male, ARV-naïve patients, in Hanoi, Vietnam for a longitudinal study of nutrition and HIV. Subjects started HAART within 2 weeks of their baseline visit. Using a repeated measures regression model they identified clinical and nutritional correlates of weight change over 2 consecutive 6-month intervals (INT1: pre-HAART to 6 months post-HAART, and INT2: 6 to 12 months post-HAART).

The mean age of participants in the study was 37±5 years and 48% reported recent illegal drug use at baseline. 81 subjects completed 6-month and 68 completed 12-month follow-up visits. 57% were started on AZT/3TC/efavirenz. Mean BMI was 19.1 kg/m^2 at baseline. Mean weight gain was 3.1±4.8 kg in INT1 and 0.7±2.7 kg in INT2. Mean CD4 change was 65±98 cells/mm3 in INT1 and 26±100 cells/mm3 in INT2. In both intervals, greater increases in CD4 and presence of nausea were both statistically significantly associated with increased weight gain (p=0.03 for both). Diarrhoea at start of interval was associated with a weight change difference of 0.3 kg in INT1 and -7.7 kg in INT2 (p=.003 for interaction). Use of liquid supplements (e.g. Ensure or sweetened condensed milk) was associated with a weight change difference of 6.5 kg in INT1 and 0.9 kg INT2 (p=0.02 for interaction).

These results suggest that use of liquid supplements, especially during the first 6 months after the initiation of therapy may be a useful intervention.

Ref: Tang A et al, Predictors of weight gain in a cohort of HIV-positive injection drug users (IDUs) initiating antiretroviral (ARV) therapy in Hanoi, Vietnam. 18th International AIDS Conference. 18-23 July, 2010. Vienna. Poster exhibition MOPE0105

http://pag.aids2010.org/Abstracts.aspx?AID=11283

Clinical and laboratory predictors of FIB-4 elevations in HCV moinofected and HCV/HIV co-infected patients

Svilen Konov, HIV i-Base

Drug users with asymptomatic chronic hepatitis C rarely have a liver biopsy to stage fibrosis. Instead, medical professionals use FIB-4, as it is a reliable, indirect marker for detecting liver fibrosis in patients with chronic hepatitis C. As many factors contribute to the progression of fibrosis and taking into account their possible differential effect, Muga A et al analysed demographic, clinical and laboratory data on FIB-4 elevations among young HCV monoinfected and HCV/HIV co-infected patients.

Participants were recruited in a unit for substance abuse treatment between 1994-2006. Socio-demographic, alcohol and drug histories and clinical characteristics were obtained trough hospital records and questionnaires. Blood samples for biochemistry, liver function tests, CD4 cell count, and serology for HIV and HCV infections were collected at admission. In order to analyse the possible predictors of FIB-4 increase, multivariate linear regression was used.

The study included 472 participants (83% male) who met the inclusion criteria. Median age of 31 years (IQR 27-35 years), median duration of injection drug use was 10 years (IQR: 5.5-15 years). Daily alcohol consumption was reported in 32% of patients and prevalence of HIV infection was 51.7% (244/472).

Median FIB-4 at admission was 0.9 (IQR 0.65- 1.46), significantly higher in the HCV/HIV co-infected patients (1.14; IQR 0.76-1.87) than in the HCV mono-infected (0.75; IQR 0.56-1.11) (p< 0.001).

In multivariate analysis, alcohol consumption (p=0.034), lower total cholesterol (p=0.042), lower albumin (p< 0.001), higher GGT (p< 0.001) and longer duration of drug use remained independently associated with a FIB-4 increase among the HCV monoinfected patients. In the co-infected, lower CD4 cell count (p=0.006), higher total bilirubin (p< 0.001), lower albumin (p< 0.001) and longer duration of drug use (p< 0.001) were statistically significantly associated with FIB-4 increase.

The data suggests that both immunodeficiency as a result of HIV, but also alcohol consumption independently impact FIB-4 elevations of HIV/HCV coinfected and HCV monoinfected people. This as a result may lead to FIB-4 related liver fibrosis.

Ref: Muga A et al, Clinical and laboratory predictors of FIB-4 elevations in HCV moinofected and HCV/HIV co-infected patients. 18th International AIDS Conference. 18-23 July, 2010. Vienna. Poster exhibition MOPE 0172

http://pag.aids2010.org/Abstracts.aspx?AID=8499

Cortisol response to stress in HIV-positive IDUs is related to depression

Svilen Konov, HIV i-Base

Even though there are much data on the link between cortisol levels and depression in several populations, its response to stress has not been thoroughly examined. In a previous study, Ownby et al showed that cortisol response to stress was related to cognitive function in HIV-positive injecting drug users (IDUs). In the study presented at the IAC, the team evaluated the relation of HIV and IDU status and depressive symptoms to cortisol response to cold pressor stress.

Serum cortisol levels were assayed at baseline and at 10, 15, 30, and 50 minutes after cold pressor stress in 110 HIV-positive and 246 HIV-negative individuals. The relation of HIV and IDU status and depressive symptoms as reported on the Beck Depression Inventory (BDI) and symptoms of fatigue on the Profile of Mood States (POMS) to serum cortisol levels were evaluated via repeated measures ANCOVA.

The results showed that both HIV-positive and IDU-positive individuals had substantially higher levels of cortisol in response to cold pressor stress, although only the effect of IDU status was statistically significant (p=0.001). Depressive symptoms were significantly related to cortisol levels (p=0.002).

The researchers concluded: "Depression in HIV-infected individuals may be related to biological markers of stress. Stress management activities in HIV-positive individuals may be useful in reducing symptoms of depression".

Ref: Ownby R et al, Cortisol response to stress in HIV+ IDUs is related to depression. 18th International AIDS Conference. 18-23 July, 2010. Vienna. Poster abstract WEPE0073
http://pag.aids2010.org/Abstracts.aspx?AID=11001

The impact of injection drug use cessation and antiretroviral therapy on smoking cessation among HIV-infected injection drug users in Baltimore, MD 1988-2008

Svilen Konov, HIV i-Base

In this study, 1022 participants of the longitudinal ALIVE study (from Baltimore, MD) who reported cigarette smoking at baseline, who were HIV-positive, and who attended at least three additional semi-annual visits from 1988-2008 were evaluated via Kaplan-Meier estimates and discrete time proportional hazards models for the relative hazards for first reported attempt to quit tobacco smoking. The study is important, as heavy tobacco smoking among HIV-positive people, and in particular IDUs, is common globally.

Despite HAART-increased survival, smoking-related morbidity in HIV-positive people is increasing.

Thirty per cent of the participants were female and the median age at baseline was 35 years [IQR=30-40]. At study entry, 87% reported current injection drug use and 52% reported smoking 1 or greater packs/day. 292 people reported at least one attempt to quit smoking (cumulative smoking cessation incidence: 41/1,000 person-years [IQR=37-46]; median age at first quit attempt: 43 years [IQR=39-46]). In multivariate analysis, recent injection drug use cessation was associated with an increased likelihood of quitting smoking (RH=2.0, 95%CI: 1.6, 2.5). Virological response to ART (RH=0.70, 95%CI: 0.52, 0.93) and increasing CD4 levels (250-350 vs. < 250 RH=0.73, (95%CI: 0.56, 0.95); 350-500 vs. < 250 RH=0.69, (95%CI: 0.53, 0.89); >500 vs. < 250 RH=0.77, (95%CI: 0.61, 0.96)) were significantly associated with a decreased likelihood of quitting smoking, as were alcohol and marijuana use.

These results clearly show that despite increased interaction with healthcare providers, HIV-positive individuals successfully receiving ART therapy appear less likely to quit smoking. Hence, HIV care providers must increase evidence-based cessation interventions to further reduce morbidity among HIV-positive people.

Ref: Ambrose BK et al, The impact of injection drug use cessation and antiretroviral therapy on smoking cessation among HIV-infected injection drug users in Baltimore, MD 1988-2008. 18th International AIDS Conference. 18-23 July, 2010. Vienna. Poster abstract WEPE0496
http://pag.aids2010.org/Abstracts.aspx?AID=7695

DRUG INTERACTIONS

Pharmacokinetic interactions between buprenorphine/ naloxone and once daily lopinavir/ritonavir

www.hiv-druginteractions.org

This study was conducted to examine the pharmacokinetic interactions between buprenorphine/naloxone and once-daily lopinavir/ritonavir (800/200 mg) in 12 HIV-negative subjects stable on buprenorphine/naloxone.

Compared to baseline vales, buprenorphine AUC (46.9 vs 46.2 ng.h/ml) and Cmax (6.54 vs 5.88 ng/ml) did not differ significantly after achieving steady state lopinavir/ritonavir. Similar analyses of norbuprenorphine (the primary metabolite of buprenorphine) demonstrated no significant difference in AUC (73.7 vs 52.7 ng.h/ml); however, Cmax was significantly decreased (5.29 vs 3.11 ng/ml, $P<0.05$) after lopinavir/ritonavir administration. Naloxone concentrations were unchanged for AUC (0.421 vs 0.374 ng.h/ml) and Cmax (0.186 vs 0.186 ng/ml). Using standardised measures, no objective opioid withdrawal was observed. The AUC and Cmin of lopinavir in this study did not differ significantly from historical controls (159.6 vs 171.3 ug.h/ml and 2.3 vs 1.3 ug/ml, respectively).

The addition of lopinavir/ritonavir to patients stable on buprenorphine/naloxone did not affect buprenorphine AUC or Cmax, but did decrease Cmax of norbuprenorphine. Naloxone concentrations were similarly unchanged. Pharmacodynamic responses indicate that the altered norbuprenorphine concentrations did not lead to opioid withdrawal. Buprenorphine/naloxone and once-daily lopinavir/ritonavir can be coadministered safely without need for dosage modification.

Ref: Bruce RD et al. J Acquir Immune Defic Syndr, 2010, **54(5):** 511-514

ACTIVIST'S OPINION

Worsening access to treatment for IDUs in the Russian Federation linked to the interruptions in ARV supply

Denis Godlevskiy, ITPCru

The problem of interruptions of ARV supplies becomes increasingly painful across the world. This is particularly relevant, knowing that in 2010 only one-third of those in need have access to treatment and even for this third, treatment is not necessarily unconditionally accessible and without interruptions. Treatment interruptions are reported from all around the world: Africa, South-East Asia, Latin America, Eastern Europe and Central Asia. Even the often perceived as a 'golden standard' in terms of access to treatment EU, had unprecedented problems in Romania. The problem did not pass by Russia either.

Interruptions of ARVs supplies in Russia started when the procurement of ART from the national budget started, namely in 2005-2006. This coincided exactly with the start of the Priority national project "Health". In the meantime the third and fourth rounds of the Global Fund also provided services in the sphere of treatment. In 2008, however, it became evident that they are not doing equally well-the treatment from the national programme started reporting supply interruptions.

The reasons for the interruptions in the supply in Russia are many and diverse and it is not my task to discuss them in this article. It is more important to realise that that interruptions happen every year and their dimensions grow, as much as the number of people who receive treatment covered by the national budget grows. And, let us face the reality, because until 2010, the interruptions were 'covered' by the pills that were received through the fouth round of the Global Fund, which ended in 2010.

The community is trying to resolve this problem in using different means today. These include: protests, proposals for improvement of the procurement and supply system, signatories letters, complaints, collecting unused pills and redistributing them, etc. Further to that, there is an ongoing monitoring of the access to ARVs.

This started in 2007-2008 by the All-Russian movement FrontAIDS with the International Treatment Preparedness Coalition in Eastern Europe and Central Asia (ITPCru). The two organisations started the project, called SIMONA+. The idea of it was to mobilise the community of PLWHA, TB, viral hepatitis and IDU to monitor the access to treatment and healthcare.

Not only formal organisations were involved in this project, but also activists who wished to contribute to the data collection. Special questionnaires were developed that were filled by activists (correspondents from different geographical areas). They covered different topics (not only HIV, but also TB, etc), but had a main focus on access to treatment. The completed questionnaires were regularly collected, the data analysed and trends described.

Thus, thanks to this project, the community, for the first time, with its own capacity, succeeded in documenting the limitations in access to treatment, especially for IDUs. The results of the first part of the project were published in the report "A Point of No Return" (2009), which was broadly distributed both within the Russian Federation and abroad. An electronic version can be downloaded as a PDF file:

http://itpcru.org/assets/files/Tochka_nevozvrata.pdf (Russian)

From December 2009 until February 2010, the second part of the project SIMONA+ was realized and the results were published in October 2010. The data reflects the situation of access to treatment in 19 Russian cities. Using structured questionnaires, 203 interviews were conducted with doctors, social workers, nurses and PLWHA.

The interviews were conducted by representatives of HIV service organisations and community-based groups of PLWHA in Biysk (Altay region), Zima (Irkutsk district), Zlatoust (Chelyabinsk district), Irkutsk, Kazan', Kaliningrad, Krasnoyarsk, Kursk, Moscow, Naberejniye Chelniy, Novorosiysk (Krasnodar region), Orenburg, Orel, Orsk (Orenburg region), Rostov on Don, Saint Petersburg, Tolyati (Samara district), Ufa and Habarovsk.

Many and diverse barriers to access to treatment were identified. The barriers included:

- Limited supply of ARVs (30% of the places where the interviews were conducted).
- Changes of the treatment regimen as a result of internal problems in the supply chain (36% of the places),
- Lack of one or more ARV medicine as a result of interruption (30% of the places).

However, the situation was particularly depressing when it comes to access for IDUs.

The survey showed that IDUs are systematically excluded from ARV treatment. The link between the exclusion and the problem of interruptions was obvious. In order not to change the regimens of patients with better adherence or "higher social status", doctors either do not start IDUs on treatment (regardless of the fact that they may need it on the basis of clinical indications), or theyexclude them from treatment programmes altogether. I will suggest that this is not an unique trait of our medical system. It is most probable that something similar will happen in any country with an epidemic that is concentrated in this highly stigmatised subpopulation when supply interruptions happen (or simply when there are not enough medicines).

In all places, where the survey was conducted, AIDS Centres use restrictions, based on social and/or behavioural criteria, when providing treatment. Those criteria go against the WHO recommendation that active use of drugs should not be a reason for exclusion from ARV treatment programmes.

In 18 (out of total of 19) places, people reported the existence of a special commission of specialists that decides whether a patient will receive or not an approval to receive ARVs. The criteria included "social incapability" and lead to discrimination of IDUs and members of other subgroups, thus violating the principle of universal right to access to treatment. We need to keep in mind that majority of HIV-positive people in the Russian Federation are still IDUs.

So, in 18 out of 19 places, a commission of doctors, who often have not seen HIV-positive patients, make decisions whether or not someone will be receiving ARVs. Commonly, the patient is forced to go through extensive tests, before the commission decides the fate of the person, as members of it are doctors who do not. By the time the commission meets, there is a period of extensive testing as members of the commission often are gynaecologists, otolaryngologists, etc., with limited or no experience in HIV. In 14 out of 19 places, the commission does not include either a social worker, or psychologist, or a peer educator who would be in position to assess the preparedness of the person to start and adhere to the therapy. In more than half of the places doctors and social workers said that dependence on recreational drugs was used as a reason to refuse ARVs.

"The personal attitude of the doctor to the patient plays a role, in other words many patients simply are not liked by the infectious disease specialist and this is reflected in their relationship, as well as affects the treatment. If the patient is an IDU, then in majority of the cases this means 'social incapacity' of the patient to the doctor". Interview with a social worker from Naberehniye Chelniy.

"We give only treatment to IDUs if they are in remission. Otherwise we recommend treatment for the drug addiction". Interview with an infectious disease doctor from Biysk, Altay Region.

"Firstly and foremost, I am interested in which stage of remission the IDU is-stable or not. It is desirable that the remission has lasted more than a year. Those IDUs who have achieved that have better chances. Then I fill in the candidacy card of the patient and send it to Kazan' for approval [by the commission]". Interview with the doctor, Naberejniye Chelniy.

As a whole, IDUs were starting treatment more rarely in 2009 than the general HIV population. So, in Kazan', from 132 treatment-naïve patients who were to start treatment only 17 were IDUs, in Novorosiysk from 35 naïve patients only 5 had experience in using drugs and in Orsk from 217-only 17.

In 2006 the Russian Federation signed a Political Declaration to Fight HIV/AIDS, taking the responsibility to provide ARVs for all in need by 2010. In addition, the Russian government increased the budget of the HIV/AIDS treatment programmes, promising to provide universal access and in 2010 took the responsibility from the GFATM for the financing and supply of all ARVs in the country. The right to health is guaranteed to every citizen of the Russian Federation by the Constitution, as well as the right to freedom from discrimination on every basis.

Unfortunately, the results from the monitoring of the access to ARVs survey allows me to make the conclusion that the aforementioned responsibilities are not met. Regardless of the statements of the government, access to ARVs in the Russian

Federation is systematically undermined by deficits of ARVs, interruptions in the supply chain and discrimination practices that exclude IDUs from HIV treatment programmes. The situation is worsened further by the fact that the Russian MoH refuses to recognise the existence of interruptions in the supply chain, which led to activists going again to the streets of Moscow in September 2010, like 6 years ago, demanding their treatment to be returned.

The results of the second stage of the project SIMONA+ can be downloaded as PDF documents:

http://itpcru.org/assets/files/Simona_rus.pdf (Russian)

and

http://itpcru.org/assets/files/Simona_engl.pdf (English)

OTHER NEWS

Independent reference group to the United Nations calls for evidence-based approach to address HIV among IDUs

Reference Group to the UN on HIV and Injecting Drug Use releases Consensus Statement of recommendations for global action

The spread of HIV among injecting drug users continues to fuel the HIV epidemic in many countries, particularly in Eastern Europe and Asia. An independent expert group to the United Nations has warned that to control the spread of HIV among injecting drug users countries must pursue evidence-based strategies that are protective of human rights.

The *Reference Group to the United Nations on HIV and Injecting Drug Use* estimates that there are 16 million injecting drug users worldwide, of whom 3 million are thought to be HIV positive.

The Reference Group recommends the implementation of *needle and syringe programmes*, *opioid substitution therapy*, *antiretroviral therapy* and *sexual risk reduction strategies* targeting injecting drug users as a matter of priority.

As reported by UNAIDS in its recent Global Report on the HIV/AIDS epidemic, many countries have managed to stabilize or achieve significant declines in rates of new HIV infections. Despite these important gains, however, HIV among injecting drug users continues to fuel the epidemic in many countries, particularly in Eastern Europe and Asia.

To achieve similar success in controlling the rapid spread of HIV among injecting drug users, it is imperative that countries pursue evidence-based strategies that are protective of human rights affirms the Reference Group in a *Consensus Statement* released today: “Interventions that violate human rights, or are not supported by evidence of their effectiveness in reducing HIV and drug related harms, should not be part of a country’s strategy to respond to HIV among people who use drugs.”

To achieve maximal impact these interventions need to be implemented together and as part of a comprehensive package of interventions to reduce the harms associated with injecting drug use. The Reference Group report that although the number of countries that have introduced these core HIV prevention services is growing, the scale of these programmes in the majority of countries is inadequate to prevent the spread of HIV among injecting drug users.

The Consensus Statement highlights the critical role of law enforcement and criminal justice systems in effectively preventing drug use related HIV transmission through working in partnership with the health sector to optimise access to HIV prevention, treatment and care for people who use drugs. Legislation and police activity should not hinder access to drug treatment services or clean injecting equipment. Effective drug treatment and HIV prevention and care should also be available to people in prison.

Acknowledging the importance of investing in drug treatment services that have been proven to reduce drug use and the risk of HIV, the Reference Group calls for the closure of “detention centres that impose arbitrary confinement and human rights abuses on drug users for ‘drug treatment’ and which offer no evidence-based treatment for drug dependence or HIV”.

Further, the Reference Group calls for “an end to the imprisonment of people who have committed no crime other than drug use or possession for personal use”.

The Consensus Statement was developed by the Reference Group at the request of the United Nations to inform the policy development and priority setting by UN agencies involved in addressing HIV and injecting drug use. The Consensus Statement draws on research examining the effectiveness of interventions to address HIV and injecting drug use and their impact in differing contexts around the world. In this Consensus Statement the Reference Group identifies key regional issues of concern and outlines recommendations for action.

The full report and summary of recommendations can be accessed online.

http://www.idurefgroup.com

The *Reference Group to the United Nations on HIV and Injecting Drug Use* was established in 2002 and provides independent advice to the United Nations system on matters related to injecting drug use and HIV. The Group consists of experts from around the world and includes researchers, clinicians and representatives from civil society organisations.

The International HIV/AIDS Alliance issues a good practice guide on harm reduction

This good practice guide is aimed at people who are developing and delivering HIV and harm reduction programmes or services at a community level in resource-poor settings, or settings where there are low levels of capacity or political support for harm reduction programmes.

The guide is for people with limited experience of HIV and harm reduction programming in a community setting. It is not a comprehensive manual containing everything that is known about successful HIV and harm reduction programming. Instead, it aims to be an accessible and user-friendly guide to thinking through what "good practice" means for community organisations working with people who use drugs. It refers the reader to many other in-depth and technical tools

people working in resource-poor settings. HIV and harm reduction programmes and services are well established in Canada, Australia and parts of Europe. But in many developing and transitional countries where HIV and harm reduction programming is urgently needed, there are added challenges of fewer resources and fewer "safety nets" or state welfare systems for people who use drugs. This affects our definitions of what are key services and programmes.

To download the guide:

http://www.aidsalliance.org/publicationsdetails.aspx?id=454

Hepatitis E vaccine candidate completely blocked disease

An investigational vaccine against hepatitis E was shown to be completely effective in a large randomised trial in China.

The trial, involving more than 100,000 patients, found that none of the patients who received the full three doses of the vaccine (HEV 239 or Hecolin) developed hepatitis E over a 12-month follow-up, according to Ning-Shao Xia, MD, of Xiamen University in Xiamen, China, and colleagues.

For further information:

http://www.medpagetoday.com/InfectiousDisease/Hepatitis/21823

A new report "Sinning and sinned against: the stigmatisation of problem drug users" by the UK Drug Policy Commission

This report aims to summarise research about the stigmatisation of problem drug users; to explore the nature of this stigmatisation, its impacts and why it happens. These considerations raise some fundamental issues about the nature of addiction and the extent to which it is seen as a moral, medical or social issue. They also raise important questions about autonomy and the blame attached to addiction.

As the title suggests, the central focus of this report is on the stigmatisation of problem drug users. However, this is not a self-evident term that comes with a common understanding. A pragmatic approach has been to define problem drug use in terms of combinations of particular drugs and modes of use: the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) defines it as "injecting drug use or long-duration/regular use of opioids, cocaine and/or amphetamines". It is this latter type of definition that has informed this report, but, to the degree that it is dependent on other studies and reports, this report has had to adopt the definitions used in these studies.

For further information:

http://www.ukdpc.org.uk/publications.shtml#Stigma_commentary

ON THE WEB

Web resources

The following organisations all include web resources about ARV4IDUs:

http://www.drugtext.org/library/legal/eu/default.htm

http://www.harmreduction.org

http://www.erowid.org

http://www.union.ic.ac.uk (see health and well-being section)

http://www.dancesafe.org

http://unaids.org

http://who.org

http://unodc.org

http://www.soros.org/initiatives/issues/health

http://www.ihra.org

http://www.hit.org.uk

http://www.opiateaddictionrx.info

The leading medical journal Lancet publishes a special issue on HIV and drug use. Those of you who are subscribers and have missed the issue may access it at:

http://www.thelancet.com/journals/laninf/issue/vol10no7/PIIS1473-3099(10)X7020-7

FUTURE MEETINGS

Conference listing

The following meetings are taking place soon:

3-7 April 2011

Harm Reduction 2011: IHRA's 22nd International Conference, Beirut, Lebanon

http://www.ihra.net/conference

23-24 May 2011

International Society for the Study of Drug Policy Annual Conference, Utrecht, The Netherlands

http://www.issdp.org/index.htm

1-3 June 2011

7th International Workshop on HIV and Hepatitis C Coinfection, Milan, Italy

http://www.virology-education.com/

A listing of international meetings compiled by the European Opiate Addiction Treatment Association in available on their website:

http://www.europad.org/events.asp

HIV i-BASE

HIV i-Base is an HIV-positive led treatment information service. We produce information both for clinicians and other health workers and for people with HIV.

Our publications are used and have been adapted in many countries and settings.

Our fully searchable website is designed to be fast to access, easy to use, and simple to navigate.

All i-Base publications are available online.

http://www.i-base.info

i-Base produce five non-technical treatment guides, which are available online as web pages and PDF files.

http://www.i-base.info/guides

- Introduction to combination therapy
- A guide to changing treatment
- Avoiding & managing side effects
- HIV, pregnancy & women's health
- Hepatitis C for People living with HIV

The site also includes a web-based Q&A section for people to ask questions about treatment:

http://www.i-base.info/questions

Recent questions include:

- What is the risk from this presciption error and taking half-dose 3TC?
- I am 54, will starting treatment protect my CD4 count?
- I am confused about my CD4 count and CD4%
- Does receiving oral sex (being sucked) possess zero risk for HIV?
- Why do the GUM clinics say to come back after 3 months if the 28 day test is negative?
- Does my partner need to use a condom if I am on efavirenz and want to become pregnant?
- I am an HIV-positive nurse. Which countries can I move to?

We have also posted online a set of generic clinic forms, developed with the Royal Free Centre for HIV Medicine, which may be a useful resource for other hospitals.

http://www.i-base.info/clinicforms

HIV i-Base

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HIV Treatment 'Passports' - Booklets for patients to record their own medical history

1 ☐ **5** ☐ **10** ☐ **25** ☐ **50** ☐ **Other** _____ _____ _____

Guide To HIV, Pregnancy and Women's Health *(January 2009)*

1 ☐ **5** ☐ **10** ☐ **25** ☐ **50** ☐ **Other** _____ _____ _____

Introduction to Combination Therapy *(July 2010)*

1 ☐ **5** ☐ **10** ☐ **25** ☐ **50** ☐ **Other** _____ _____ _____

Changing Treatment and Drug Resistance *(February 2011)*

1 ☐ **5** ☐ **10** ☐ **25** ☐ **50** ☐ **Other** _____ _____ _____

HIV and Quality of Life: Guide To Side Effects and other Complications *(December 2010)*

1 ☐ **5** ☐ **10** ☐ **25** ☐ **50** ☐ **Other** _____ _____ _____

Guide to HIV and Hepatitis C coinfection *(March 2009)*

1 ☐ **5** ☐ **10** ☐ **25** ☐ **50** ☐ **Other** _____ _____ _____

Earlier versions of many treatment guides are available in other languages as PDF files on the website

Adherence planners and side effect diary sheets - In pads of 50 sheets for adherence support

1 Sheet ☐ **1 pad** ☐ **5 pads** ☐ **10 pads** ☐ **Other** ☐ _____ _____

Please fax this form back, post to the above address, or email a request to HIV i-Base:

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