MEETING ABSTRACTS

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ORAL PRESENTATIONS

EPIDEMIOLOGY, SUBTYPES, REGIONAL ISSUES, FOCUS ON HIV INFECTION IN WOMEN, MTC TRANSMISSION

O1 Current epidemiological HIV/AIDS situation in Republic of Moldova
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In Republic of Moldova during 1987-2013, there were 8557 reported HIV+ cases, of which 2464 (28.8%) developed AIDS, 1752 (20.5%) died. Newly, 700-750 HIV positive cases are registered per year. The biggest number of HIV+ is found at the age 25-39.

In relation to the way of transmission, the majority are infected by heterosexual contacts with tendency of increase, from 5.7% in 2000 to 91.4%. The next is among intravenous drug users (IDUs) with tendency of decrease from 83.7% in 2000 to 5% in 2013.

There are 5249 HIV+ persons in active evidence (77.13% of those who are alive), 3781 men and 3024 women. Of these, 2493 persons, including 82 children are currently on antiretroviral treatment.

The incidence in 2013 was 17.99 per 100,000 population, in the eastern regions – 46.91.

The prevalence at January 1, 2014 constituted 173.43 per 100,000 population, in the eastern regions – 463.25. The large number of HIV newly infected cases in the east territories can be explained through limited access of the population to the prevention programmes, including population with high risk of infection.

Every year, there are registered about 80-90 cases of HIV infection among pregnant women. The rate of mother to child transmission in 2013 was 1.9%. The Integrated Bio-Behavioral Study in key populations at higher risk was done in 2012-2013. From IDUs living in Chişinău, during the last year, 47.3% of the respondents took an HIV test and knew the result of the last test. HIV prevalence was 8.5% (16.4 in 2009).

From commercial sex workers living in Chişinău, during the last year 22.1% of respondents reported having taken an HIV test and knowing the result. HIV prevalence was 11.6% (6.1 in 2009).

From men who have sex with men, living in Chişinău, during the last year, 24.3% of the respondents took an HIV test and knew the result of the last test. HIV prevalence was 5.4% (1.7 in 2009).

The Republic of Moldova is classified as a concentrated/low prevalence country with a concentrated HIV epidemic in key populations such as injecting drug users and their regular sexual partners, commercial sex workers and men who have sex with men and there is an evidence of spread of the infection in the general population.

O2 First case of recent retroviral infection after accidental occupational non-medical exposure to contaminated HIV blood in National Institute for Infectious Diseases “Prof. Dr. Matei Baţ” Bucharest, Romania
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In 2013, in the National Institute for Infectious Diseases “Prof. Dr. Matei Baţ” Bucharest has been applied post-exposure guidelines in 112 cases of occupational exposure to blood and other biological products and was not registered any cases of HIV transmission.

A 22 year old, young police-officer presented in our service for human bite wounds, resulting from intervention in a case of intrafamilial aggression. The aggressor, was known as drug-addicted, co-infected HCV/HIV and he had bleeding in the mouth. He was under antiretroviral therapy for about nine months (CBV+NVP, viral load = 90.787 copies/mL, CD4 = 200 cells/μm, HCV-RNA = 6,718,917 IU/mL). Exposed person comes to our service in the first two hours of the incident, without performing initial wound toilet. We started antiretroviral prophylaxis (ARVP) with CBV+LPV/r.

At eight days after ARVP, the exposed-person developed a generalized maculopapular rash; in the absence of other clinical manifestations the eruption is interpreted as post-drug side effects. The young man returned to our clinic after another three days (range in which in his own initiative
stopped prophylaxis), and we decided to change the antiretroviral regimen with DRV/r + TDF + FTC. Reevaluation after a month recorded that he remained asymptomatic and fourth generation ELISA tests were negative. Reassessment at 12 weeks showed serological tests positive (ELISA, Western blot -p24 = + + +), indicating a recent retroviral infection. We find the same HIV sub-type (F) and the same resistance mutations in those two patients, confirming HIV infection to policeman from the aggressor. New patient initially had HIV-RNA = 210,977 copies/mL, CD4 = 789 cells/cmm and was included in the cohort of individuals with recent HIV infection; antiretroviral therapy is initiated with TDF + DRV/r + RAL. After a month of treatment the HIV-RNA = 161 copies/mL blood, HIV-RNA from CFS was undetectable and anti-HCV were negative. It is the first case of accidental post-exposure (medical and non-medical) to contaminated blood HIV infection in which we applied post-exposure protocol. It illustrates:
- The importance of adherence to antiretroviral medication;
- The consideration of acute retroviral syndrome in the presence of a maculopapular rash;
- The importance of choosing prophylactic regimen when we know treatment history and possible resistance mutations if the source person is known to be HIV positive;
- Should be monitored more frequently and more complete (HIV-RNA), including people with occupational non-medical exposure.

**O3**

The dynamics of HIV trends of transmission in the Romanian cohort

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Since the early 1990s Romania has made important progresses in the HIV/AIDS area, also recognised by the international community. These steps forward concern treatment and care for people living with HIV/AIDS (PLWHA) and prevention of HIV transmission among young people and vulnerable groups. However, the global economic crisis has generated a behavioural change especially among the young population, with an increase of incidence at 2.54/100,000 (31 December 2013). At the end of 2013 we performed the annual statistical evaluation of the HIV epidemic. The National Database registered 19,261 cases of HIV and AIDS (cumulative total 1985-2013), of which 12,273 were PLWHA. Most cases (65%) were diagnosed when they were children (<14) at the beginning of the 1990s and since then have experienced multiple ART regimens and reached a fertile age. Most of the new registered cases (797) represent young PLWHA (20-24, 25-29) who suffered changes in their behavioural patterns. Hence, the former intravenous drug users (IDUs) shifted to daily use of new drugs (ethnobotanicals) while young women acquired HIV through unprotected sex and intravenous drug use.

Another area of concern was mother to child transmission of HIV that we assessed in the context of prenatal and postnatal cares. Since 2011, the national response to HIV has weakened as a consequence of the economy. Hence, the new IDU-HIV cases boosted from 14 cases (3%) in 2010 to 233 (29.23%) in 2013. At the same time we detected a growth in the share of children born from women using drugs, including women living with HIV/AIDS (WHLA). For the same category we identified 76.83% HCV co-infections, 11% HBV-HCV co-infections. The assessment evinced that late presenters account for more than 50% from the new cases, with CD4=350 cells/cmm. In addition, 32% of patients in treatment have low CD4 counts <350 cells/cmm (end 2013). The rising number of pregnant women addicted to drugs is directly proportional to the expanding figures of drugs and new drug users. Cares provided to newborns from mothers who use i.v. drugs and new drugs, perinatally exposed to HIV are usually associated with hepatitis B, C and with syphilis.

Romania needs an upgrade of its national HIV/AIDS policies: broaden access to treatment and integrated services, using ART as prevention measure to avoid HIV transmission among the general population and a strengthened partnership between the medical networks, in order to respond to the emergent HIV trends.

**O4**

The challenges of managing antiretroviral treatment in children perinatally infected with HIV in Romania

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In the past few years, the rate of HIV perinatally exposed children has increased as a consequence of the expanding number of infected women. These women belong, on the one hand, to Romania’s 1990s cohort, and on the other to the group of new sexually or intravenously (i.v.) drug infected women. To report the characteristics of vertically HIV infected children in the last six years in Romania, to investigate temporal trends in their evolution with antiretroviral treatment and to characterize the causes of treatment failure in these children.

Children with perinatally acquired HIV infection were followed in a retrospective case series. The cohort included 43 children, evaluated in the National Institute of Infectious Diseases "Prof. Dr. Matei Balș", born between 2008-2013, from 86 HIV infected children under 6 years, in active records in Romania. We assessed maternal characteristics, HIV vertical transmission prophylaxis, timing of diagnosis, immunological and virological status, features of the evolution of these children with ART. 43 perinatal HIV infected children were evaluated in our clinic from 396 perinatally exposed children, with a rate of transmission of HIV infection of 10.8%. 16% of mothers belonged to the Romanian ‘90s cohort and 84% were recently infected with HIV, sexually or through i.v. drug use. 41% of the subjects were diagnosed with HIV infection at birth. Their median entry CD4% was 23% and 49% had a CD4 >25%; median entry viral load was 7 log. 16 patients (37%) had undetectable viral load after six months of treatment. In 87.5% of them, the virologic suppression was achieved and maintained with one single regimen (2 NRTIs + 1 NNRTI or 2 NRTIs + 1 PI/r).

15 children (35%) had never achieved suppression of viral load to undetectable levels. 19 children (44%) faced special issues related to adherence to antiretroviral treatment. The management of antiretroviral treatment in children with vertically acquired HIV infection is challenging, due to limited therapeutic options, lack of adherence, drug interactions and adverse events.

**O5**

Molecular diversity of HIV-1 in Croatia

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Croatia is a small southeastern European country with a low prevalence of HIV infection and a centralized system of clinical care. The cumulative number of HIV infections in the period 1985-2013 was 1,102. The aim of this study was to analyze the distribution of HIV-1 subtypes in Croatia. The study enrolled 356 HIV-infected patients (86.2% males) receiving clinical care at the Croatian Reference Center for HIV/AIDS in the period 2000-2013. The patients were classified into three groups based on the year of genotyping and entrance to clinical care (2000-2005, 2006-2010 and 2011-2013). Population-based sequencing of the 3’ part of the pol gene was performed by using TRUGENE® HIV-1 Genotyping System. HIV-1 subtypes were determined by HIV REGA Subtyping Tool.

Subtype B was detected in 279 of 356 patients (78.37%). In the period 2000-2005, a total of 28.3% (47/166) of patients were infected with non-B subtypes. More recently, percentages of non-B subtypes decreased to 14.9% (20/134 patients, 2006-2010) and 17.8% (10 of 56 patients,
2011-2013. Non-B subtypes were detected in 27 of 49 (55.1%) HIV-infected women. A total of 93.1% (175/188) men who have sex with men (MSM) patients were infected with subtype B. The majority of HIV-1 infections in Croatia can be attributed to subtype B, particularly among MSM. Non-B subtypes are associated mainly with heterosexual transmission.

O6 Mother to child transmission (MTCT) of HIV - almost a thing of the past? A cohort study of HIV positive women starting antiretroviral drugs in pregnancy

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Where available, antiretrovirals (ARVs) and antenatal HIV testing and care have significantly reduced mother to child transmission (MTCT). Higher maternal viral load (VL) is linked with higher risk of MTCT, increasing risk of MTCT for women starting ARVs during pregnancy compared to those already suppressed.

A single-centre, retrospective cohort of women starting ARVs during pregnancy from 2004 till 2013. Demographic, obstetric and virological data, and neonatal outcomes were collected where available.

60 pregnancies were recorded (in 56 women) in which ARVs were started or restarted from a total of 129 recorded pregnancies. 48% (27/56) were new antenatal HIV diagnoses and in these median gestational age (GA) at diagnosis was 16.1 weeks (range 5.3-37.6). Median GA at ARV commencement was 22.4 weeks (range 8-37.7) with 63% (35/56) starting before 24 weeks and 91% (51/56) before 28 weeks. HIV diagnosis during pregnancy was associated with a later commencement of ARVs (23.9 vs 19.9 weeks, p=0.009). The ARV regimen was available for 58 pregnancies. Treatment was with two NRTIs plus NNRTI (3), or PI (54) or raltegravir (1). Raltegravir was added as a forth agent in 7 patients. 87% (52/60) had resistance genotyping before (14) or during (38) pregnancy, 81% (22/27) for new diagnoses in pregnancy. The rate of any ARV resistance was 12% (6/52): 4 patients had NNRTI and 2 NRTI resistance mutations, 4 were treatment-naïve. This was not associated with birth defects. HIV VL at delivery was available in 57 pregnancies with detectable VL in 16% (9/57). Pre-treatment VL >100,000 copies/mL during pregnancy was associated with higher risk of detectable VL at delivery (p=0.016), 69% babies were delivered by Caesarean section, 32% as an emergency. There was one late miscarriage at 17 weeks. Median GA at birth was 38 weeks (range 17-42) with 21% born at <37 weeks (10/48). There was one HIV MTCT (1.7% for those starting ARV in pregnancy, 0.8% overall) in a woman who was poorly adherent with ARVs throughout pregnancy with a VL of 216 copies/mL at delivery following a period of directly observed therapy.

Over 10 years of integrated HIV and antenatal care, there was only one case of MTCT. Initiating ART for prevention of MTCT is complex, requires a multi-disciplinary approach and importantly patient engagement. Antenatal practices and guidelines have changed over the period of this dataset, allowing normalisation of pregnancy when HIV is diagnosed and treated early.

COMORBIDITIES, AGEING WITH HIV

O7 Birth defects in HIV vertically exposed children

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Objective: to identify types of birth defects in HIV vertically exposed children and to determine the rate of congenital disorders counted in children born to HIV infected mothers.

We analyzed the data recorded for HIV perinatally exposed children followed up in the National Institute for Infectious Diseases “Prof. Dr. Matei Balș”, Bucharest, the Pediatric Department from January 1st 2006 to December 31st 2012. Of 203 children with data on clinical, imagistic and virologic aspects, 20% were diagnosed with HIV infection and more than 33% had at least one congenital condition. The birth defects identified in studied children were: congenital heart defects 63%, musculoskeletal defects 23%, renal malformations 10%; neurologic defects 10%, digestive tract malformations 5%; metabolic and storage disorders 2% and genetic disorders 2%. 9% from studied children with birth defects had more than one organ involvement. Among HIV infected children the most frequent congenital disease was heart malformation, followed by renal and neurologic malformations. In total less than 30% from HIV vertical infected children and more than 33% HIV exposed but negative children had congenital diseases. The difference is not statistically significant (p=0.38). Comparing the group of children born by treated mothers to those from untreated mothers we have noticed that the use of antiretrovirals during or before pregnancy is not associated with malformations (p=0.45). In the same time the risk of congenital diseases in our patients is associated with mothers being part of Romanian cohort (p=0.05). The relative risk to have malformations in the second generation of Romanian cohort is 1.49 higher comparing with children born by more recently infected mothers. We also found very rare congenital diseases: chromosomal hermaphroditism, gangliosidosis and Niemann Pick syndrome (less than 1/100,000 live births). The rate of malformations is relatively high among HIV exposed children compared with general population in Romania and it was associated with long history of HIV disease (Romanian cohort).

O8 Antiretroviral therapy adherence monitoring and its impact on immuno-virological outcome

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One of the most important factors in achieving a good outcome is treatment adherence. Poor adherence to antiretroviral therapy (ART) leads to less viral suppression, permanent treatment resistance and increased costs. There are multiple causes of poor adherence: regimen complexity, side effects etc. Aim: to analyze ART adherence, risk factors for poor adherence and their impact on the outcome.

We performed a one year survey (from January to December 2013) of HIV infected patients monitored in the Third Department of the National Institute for Infectious Diseases “Prof. Dr. Matei Balș”. The data (number of days covered by ART) was collected from patients’ files. We correlated the adherence with gender, regimen rank and complexity. Statistical analysis was made using EPI INFO 6. We retrospectively analyzed 111 patients who came in to our clinic monthly to pick-up their ART, 52 women (46.84%) and 59 men (53.16%) with a mean age of 43.5 years old. The adherence to ART was: 23 (20.62%) – 100% adherence, 36 (32.43%) – more than 96.7% adherence (less than 12 days without medication), 38 (34.23%) – 91.8% to 96.7% adherence (13-30 days without medication), 10 (9%) – 83.6% to 91.8% adherence (30-60 days without medication) and 4 (3.6%) with less than 83.6% adherence (more than 60 days without medication). The level of adherence was correlated with therapeutic failure: for 100% adherence – two failures (8.69%), for more than 96.7% adherence – no failure, for
more than 91.8% adherence – 4 failures (11.1%), for more than 83.6% adherence – 2 failures (20%) and for less than 80% adherence – 3 failures (75%). Adherence below 91.8% was correlated with treatment failure: RR 5.65 (C195% 1.99; 16.09, p=0.0007). We analyzed some possible risk factors for poor adherence: gender, regimen rank and complexity. Although 51.95% from the non-adherence group were women, the adherence wasn’t correlated with gender: RR 1.23 (C195% 0.93; 1.62, p=0.16). A regimen rank higher than 1 was correlated with low adherence – 45.76% vs. 28.84% in the adherence vs. non-adherence group: RR 1.5 (C195% 0.95; 2.36, p=0.07). The regimen containing protease inhibitors wasn’t correlated with low adherence: 33.9% vs. 30.8%, RR 1.08 (C95% 0.71; 1.67, p=0.73).

We emphasize the impact of therapy adherence on the outcome. A level of adherence below 91% was correlated with therapeutic failure. ART adherence wasn’t correlated with gender, PI regimen and rank regimen.

O9  
Low level viraemia and the risk of virological failure in HIV infected patients
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Objective: to estimate the rate and the significance of low level viraemia in HIV positive patients registered in the National Institute for Infectious Diseases “Prof. Dr. Matei Balș”, Bucharest, Romania. We retrospectively analysed the rate of HIV viral loads (VL) <200 copies/ml in patients admitted in our institute from 2011 to 2013. The patients with undetectable VLs in 2011 and low level VL in 2012 were selected and divided into three groups, according to their HIV RNA (<40, 41-50 and 51-200 copies/ml, respectively). We evaluated for each group the risk of virological failure (VL>200 and >1000 copies/ml) over a 12 months period.

A low level VL was detected in 16.2% of the 3,916 evaluated patients, the rate of HIV RNA of 51-200 copies/ml being two times higher than the rate of a VL <50 copies/ml. A number of 84 patients had a VL<200 copies/ml after being HIV RNA undetectable. In these patients the risk of virological failure over a 12 months period was not correlated with the HIV VL group or the used antiretroviral regimen (protease inhibitors PI vs. non-PI containing regimen).

A low level viraemia is a rather common event in the studied HIV patients. In previously undetectable patients a HIV RNA <200 copies/mL is not associated with an increased risk of virological failure in the next year.

O10  
Antiretroviral treatment in adult ethnobotanical intravenous drug users recently infected with HIV
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During the last few years in Romania, increased numbers of new HIV infections among ethnobotanical intravenous drug users (eIVDU) were observed. Although most cases have relatively good immunological status, some patients claim antiretroviral (ARV) treatment because of very low CD4 count, severe comorbidities and/or pregnancies despite difficulties related to their adherence.

Retrospective analysis of 32 patients, eIVDU, treated with ARV in our hospital between 1th January 2010 and 31th January 2014. From all 32 patients, 27 are males (84.4%). The main reason for starting ARV treatment was represented by severe AIDS-defining illness (71.4%) related to immunodepression with CD4 count below 100 cells/cmm 11 cases (34.3%) and one pregnancy. In our study group the mean CD4 count at baseline was of 110.1 cells/cmm (median CD4 102.5 cells/cmm). 24 patients (75%) received at first triple therapy including NNRTI (10 cases with nevirapine, 14 cases with efavirenz), the other 8 patients (25%) received from the beginning regimens with protease inhibitors. 7 patients from the first group were then switched to protease inhibitors, mostly after completing tuberculostatic treatment, while 2 patients from the second group were switched to integrase inhibitors because of potential drug-drug interactions involving rifampin. All patients in our study were coinfected with HCV, 9 patients (28.6%) had also HBV, and 15 patients (46.8%) had active tuberculosis. Only 15 patients were truly adherent to ARV (43.7%); we registered 5 cases of abandonment and one death. From all 5 patients who discontinued treatment 3 were social cases; from all 28 patients who are currently treated 20 have good family support (71.4%) and 6 (21.4%) receive psychological counseling and methadone substitution therapy. Mean value of CD4 count at 1 month of HAART therapy was of 225.8 cells/cmm, probably related to ARV treatment received correctly during admission in our clinic, but this value decreased to 213.3 cells/cmm at 3 months, probably related to poor compliance at home.

Despite the fact that they are recently infected with HIV, increasingly more eIVDU patients are in need of ARV treatment, because mainly of rapid immunodepression and comorbidities associated with AIDS. Family support as well as psychological counseling and substitution therapy with methadone are mandatory for achieving clinical success with HAART, while lack of adherence is the principal cause for immunological and virological failure. Tuberculosis with both pulmonary and extrapulmonary involvement is the principal complication associated with AIDS, involving almost half of the eIVDU in our country.

O11  
Variation in CD4 cell count among IDUs versus sexually-infected HIV-positive naïve patients in Romania
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Since 2011 Romania is experiencing a dramatic increase of newly diagnosed HIV infections among injecting drug users (IDUs), mainly linked to the introduction of new psychoactive substances (NPS) on the Romanian market, their use being related to higher levels of risk behavior compared to opioid abuse. There is no sufficient data showing the natural course of HIV in subjects infected through IDU – the majority are ART-naïve due to recently acquired infection (many are asymptomatic and have a CD4 cell count over 350 cells/cmm) and poor adherence. Our objective was to determine if IDUs have a faster decline in CD4 cells than sexually-infected patients.

We performed a retrospective study, including ART-naïve HIV-positive patients diagnosed between January 2011 and June 2013 at the National Institute for Infectious Diseases “Prof. Dr. Matei Balș”, who had 2 subsequent CD4 cell count determinations over a timespan of 6-24 months and a baseline CD4 count higher than 350 cells/cmm. Among 1,248 newly diagnosed patients, 234 met these inclusion criteria. The data were statistically analyzed using SPSS version 17 (independent sample t-test, Mann-Whitney test, linear regression; the significance level was set at 0.05).

The majority (80%, 187/234) were men and the median age was 29 years (15-76). More than half of the patients (138; 59%) were former or active IDUs, with low socioeconomic status, most of them injecting both opioids and NPS and 55 (40%) of them were in detention at the moment of HIV diagnosis. Among them, 98% were coinfected with HCV, as opposed to only 21% of the sexually-infected patients. Subtype analysis was performed for 64 patients and revealed the following subtypes and circulating recombinant forms (CRF): 50 F1, 3 B, 10 CRF14_BG and 1 CRF14_F. There was no significant difference of CD4 cell count between the two groups at baseline (p=0.55). The median variation of CD4 cells in IDUs was 150 and 42 in the non IDUs group. IDUs had a statistically significant CD4 cell decline (p=0.01). HCV coinfection was also correlated with a faster decline in CD4 cells (p <0.001).
Leptin is a hormone secreted by the adipose tissue that may be associated in the general population with components of the metabolic syndrome (MS). Our objective was to test the association between dyslipidemia, MS presence and circulating leptin dysfunction in a cohort of HIV-infected non-diabetic patients undergoing combinator antiretroviral therapy (cART).

We included HIV-infected non-diabetic consecutive patients undergoing cART, admitted to the National Institute for Infectious Diseases “Prof. Dr. Matei Balș”, between 2008-2011. The diagnosis of MS was made using the International Diabetes and American Heart Association harmonized criteria from 2009. Circulating levels of leptin (BioSource EASIA) were measured.

We enrolled 95 patients: 53 (55.8%) males (mean age=33.1±13.4 years) and 42 (44.2%) females (mean age=30.5±13.6 years). Most patients (72.5%) had undetectable HIV viral load; median CD4 count was 305 (IQR=302-308) cells/µl. The median time on cART was 38.5 (IQR=37-40) months. 38.8% of patients had experienced more than one cART regimen.

The prevalence of MS was 17.1%. Elevated blood pressure, elevated waist circumference and abnormal fasting glucose prevalences were 30.3%, 17.1% and 6.5%, respectively.

Median serum leptin was 1.89 (IQR=1.57) ng/mL. Circulating leptin dysfunction was present in almost half of patients, hypoleptinemia being more frequent (42.2%) than hyperleptinemia (8.5%).

Hypoleptinemia was more frequent in men (62.3%) comparative to women (17.1%) p=0.000. The prevalence of MS in patients with hypoleptinemia was 25.8% vs 10.8% in persons with normal leptin values (p=0.261). Hypoleptinemia was associated with elevated waist circumference (p=0.004) and abnormal fasting glucose (p=0.005) in men. More than half (65.6%) of men with hypoleptinemia had reduced HDL-cholesterol levels vs 29.4% in men with normal levels of leptin. As expected, hyperleptinemia was associated with the increase of body mass index, both in men (p=0.000) and women (p=0.005).

In our cohort of young cART multiexperienced HIV patients leptin dysfunction was not significantly associated with MS presence. Leptin was correlated with several MS components (HDL-dyslipidemia, elevated circumference, abnormal fasting glucose) with significant gender differences, that suggests that leptin may play different roles in the regulation of glucose and lipid metabolism according to the sex.
Hepatitis B virus (HBV) infection is common in individuals infected with human immunodeficiency virus, and co-infection is associated with higher rates of HBV replication and more rapid liver disease progression than HBV monoinfection. This study evaluates the prevalence and virological profiles of hepatitis B infection in a cohort of long term survivors, with multiple antiretroviral treatments. 164 HIV-infected subjects (median age: 24 years) on combined antiretroviral therapy (cART) (median duration: 13 years), were evaluated for serologic markers of HBV infection (HBsAg, total anti-HBc and anti-HBsAg antibodies). Markers of HBV infectivity (HBeAg and HBV DNA) were evaluated in all HBsAg carriers; HBV genotype and lamivudine resistance mutations were analyzed in the cases with HBV DNA >10^4 IU/mL. 65.9% of the patients (108/164) had markers of past or present HBV infection (antiHBc positives), out of which 51.8% (56/108) were chronic HBV carriers and 30.5% had resolved HBV infection. All subjects were equally exposed to HBV infection, irrespective of their current immune status. Out of 21 patients with isolated anti-HBc antibodies, only 4 had detectable HBV DNA, presumably having occult hepatitis B. HBV chronic carriage rate was not influenced by the immune status. Overall, only 17.8% of the chronic carriers had active HBV replication; severely immune-depressed patients tend to maintain active viral replication more frequently than those with moderate or absent immunosuppression. The majority of the coinfected individuals (68.3%) showed no sign of liver fibrosis (APRI score <0.5), only 3% had severe fibrosis (APRI score >1.5); HBV DNA was directly correlated with APRI score. HBV genotype A was present in all but one of the tested patients. 98.8% of the coinfected subjects have been treated with a cART regimen that includes a drug dual active against HIV and HBV (in 98% of the cases lamivudine (3TC), for a mean time of 6.9 years and in 29.7% of the cases the current dually active drug was tenofovir). 3TC-resistance mutations were present in only 4 coinfected subjects. We found a strikingly low percentage of long term HIV/HBV coinfected patients from our group with active liver disease. A high prevalence of asymptomatic HBV chronic carriage was associated with a good immune status, suggesting that dually active antiretrovirals have an important role in delaying progression of liver disease in HIV/HBV coinfected patients.

O17 Influence of liver fibrosis stage on nevirapine plasma concentration in HIV-infected patients with chronic hepatitis C virus
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Hepatitis C virus (HCV) co-infection in HIV positive patients can affect the pharmacokinetics (PK) of antiretroviral drugs that are metabolized by the liver. Therefore, we determined plasma nevirapine (NVP) concentrations (C_{\text{trough}}) in HIV+ patients with or without HCV co-infection. This was a prospective study in patients receiving NVP (200 mg twice daily or 400 mg once daily) for at least 12 weeks as a part of antiretroviral regimen, at the HIV/AIDS Centre, Infective and Tropical Disease Clinic, Belgrade, Serbia. Written consent was obtained and the study was approved by the local ethics committee. NVP plasma concentrations were measured by a validated HPLC-UV method at the University of Liverpool, UK. Statistical analysis was performed by SPSS software package. 27 patients (18 HIV mono-infected and 9 HCV/HIV co-infected patients) receiving NVP as part of their antiretroviral therapy were enrolled. The median age of the 27 patients was 43 years and all were Caucasian. In all patients HIV RNA was <50 copies/ml; median CD4+ T-cells count was 363 cells/cmm. Median NVP C_{\text{trough}} was 4826 ng/ml (2533-8718 ng/ml) in the HIV mono-infected group and 5810 ng/ml (4995-11783 ng/ml) in the...
HIV/HCV co-infected group, respectively. Compared to an individual with HIV mono-infection, those with HCV/HIV co-infection had a higher NVP trough level (95%CI +67 ng/mL, +2940 ng/mL; P=0.03). NVP plasma levels above the toxic threshold (8000 ng/mL) were more frequent in patients with liver cirrhosis than in those without (33% vs. 4%; P <0.001). Despite the small numbers of patients included, this PK study has shown that NVP plasma levels are impaired in HIV-infected patients co-infected with HCV, especially in those with liver fibrosis.

**O18**

**Co-infection with hepatitis C virus (HCV) in Estonian intravenous drug users HIV epidemic**

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**BMC Infectious Diseases 2014, 14(Suppl 4):O18**

Estonian concentrated HIV epidemic started in August 2000 when rare HIV-1 CRF06_cpx was introduced into the population of intravenous drug users (IDUs). The majority of these HIV-positive subjects are likely co-infected with HCV but the prevalence of HCV and its genotypes during HIV concentrated epidemic in Estonia is largely unknown. The Estonian HIV database collects clinical and laboratory data (including HCV) of HIV-positive patients on medical care. Of 4500 patients on medical care 3300 are entered into Estonian HIV database (in total 8664 diagnosed).

Aim: to describe the prevalence of HCV infection and the distribution of the HCV genotypes among HIV-positive subjects infected during HIV concentrated epidemic in Estonia.

Data for present analyses was extracted from Estonian HIV database on 2nd of January 2014 and it comprised subjects diagnosed HIV-positive from 2000.

In total, 2,420 of 3,476 (70%) HIV-positive subjects were HCV antibody positive and 1,184 (64%) were HCV RNA positive. More than half of HCV positives were men (66%) and the median age was 32 years (inter quartile range 30-36) y. The prevalence of HCV was higher in subjects verified to be HIV-positive between 2002 and 2010 as compared to between 2011 and 2013 (90% – 66% in 2002 – 2010 vs 50% – 45% in 2011 – 2013; p <0.05). The prevalence of HCV-positivity was equally high in subjects reporting the use of intravenous drugs (88%), the use of other narcotics but intravenous drugs (69%) and persons who have not reported the use of illegal drugs (71%). In total 640 subjects had HCV genotype data available. The dominating genotypes were Ib (53%) and IIA (36%), however, in recent years the prevalence of genotype la is raising (from 2.6% in 2005 to 25% in 2013). The distribution of HCV genotypes between different IDUs and non-IDUs was similar. Altogether 5% of HCV RNA positive subjects (66% with genotype Ib or IIA; 29% with mixed or unknown; 5% with la or I) received HCV treatment and all except one admitted the drug usage. Of 59 subjects 48 (81%) received both HCV and HIV therapy.

Decreased prevalence of HCV-positive subjects among HIV-positives may suggest a lowered HIV transmission through intravenous route during the last years. The high prevalence of HCV in persons who did not report the use of illegal drugs might indicate under-reported drug usage in this population.

**O19**

**Concordance between noninvasive assessments of fibrosis in patients with HIV/HCV co-infection**

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Many studies used non-invasive methods to estimate the prevalence of significant fibrosis and its risk factors in patients with HIV infection. We evaluated the ability of APRI and FIB-4 score to differentiate between the different stages of fibrosis (no fibrosis/minimal fibrosis = F0-F1 and F2-F4 fibrosis moderate-severe/cirrhosis), taking as a reference, in the absence of liver biopsy, the hepatic fibrosis stratification by FibroScan. Group 1 was represented by 39 patients with HIV infection and group 2 by 71 patients with HIV/HBV coinfection. AUROC was used to calculate for each group and for each score the optimal value for identifying significant fibrosis. Then we determined the cut-off value that identifies significant fibrosis with maximum specificity. The Kappa score was then calculated for the concordance between methods.

For HIV/HBV coinfected patients, to identify significant fibrosis score on the classification of fibrosis by APRI versus FibroScan, Kappa=0.494, 95% CI (0.245, 0.742) on the identification of fibrosis (F0-F1 to F ≥2), for the FIB-4 Kappa=0.481, 95% CI (0.238, 0.725) for both the moderate-concordance. Regarding the comparison of the two methods APRI and FIB-4 kappa=0.698, 95% CI (0.485, 0.910), significant concordance.

For patients with HIV to identify significant fibrosis Kappa score tally on the classification of fibrosis by APRI versus FibroScan Kappa=0.217, 95% CI (-0.424, 0.858) on the identification of fibrosis (F0-F1 to F ≥2), for the FIB-4 Kappa=0.164, 95% CI (-0.451, 0.779) for both the correlation is reduced. Regarding the comparison of the two methods APRI and FIB-4 kappa=0.217, 95% CI (-0.424, 0.858), which confirms the low correlation.

There is sufficient evidence that the tests used: APRI and FIB-4 have the ability to distinguish for both groups of patients between the two classes of fibrosis (F0-F1 to F ≥2) meaning between patients with and without liver disease.

Although for patients with HIV infection a low concordance was noted between non-invasive methods for the diagnosis of fibrosis, in coinfected patients it was moderate and these tests could be used as evaluation methods in the monitoring of liver injury especially when the results of these tests are concordant.

**RESISTANCE, TROPISM, LABORATORY MONITORING**

**O20**

**Baseline HIV-1 tropism prediction in advanced immune suppressed patients: evidence of CXCR4 viruses in IDUs infected with recombinant forms**

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Until 2011, the main risk factor for the spread of HIV-1 in Romanian adult population was heterosexual contact. More recently, the number of HIV-1 new cases among IDUs significantly increased. This new subepidemic is characterized by circulation of particular forms of infective strains (CRF14_BG, high prevalence of HCV co-infections and infective endocarditis. Genotypic methods are currently used for testing viral tropism in HIV infected patients. Deep sequencing proved to have much higher sensitivity than population sequencing in detecting minority - CXCR4 tropic viruses. Previous studies suggested that the presence of CXCR4 phenotype at baseline is frequently associated with a faster disease progression. The aim of the study was to evaluate the viral tropism at the moment of HIV diagnostic in IDU patients.

We have analyzed sequences from 19 IDUs that presented low CD4 counts (<200 cells/cmm) and/or CDC stage C when HIV-1 infection was diagnosed. They were compared with strains from 24 heterosexuals diagnosed at the same time with the IDUs were included in the study. RT PCR was performed to amplify the V3 loop. Population sequencing was done using BigDye chemistry and 3100 Genetic Analyzer. Deep-sequencing was performed on the GS Junior 454 sequencing platform and AVA software was used to analyze the output sequences. The tropism prediction was assessed by geno2pheno [coreceptor] bioinformatic algorithm and subtyping with REGA tool version 2.0. The IDU group was mainly infected with recombinant forms: CRF14_BG and recombinants between F1 and CRF14_BG (68.4%, 13/19); the heterosexuals had F1 subtype viruses (95.8%, 23/24). CRF14_BG tropism was found in all IDUs and in particular with CRF14_BG (p=0.0027). All the CRF14_BG were X4 by population sequencing. Furthermore, when tested with deep sequencing the viral populations of CRF14_BG samples were exclusively X4 (no minority R5 populations). Dual tropic (CCR5 and CXCR4) populations were more frequent in F1 samples isolated from heterosexuals and predicted as X4 by population sequencing. We found concordance between the predictions of
the two methods. In the heterosexual group both techniques predicted mainly CCR5 viruses. CXCR4 tropic CRF14_BG viruses were very common in IDUs at baseline. This may contribute to faster disease progression in this population than in heterosexuals infected with the F1 CCR5 tropic strains.

**O21**

**Forensic application of phylogenetic analysis – exploration of suspected epidemiological linkage**

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Phylogenetic analysis may serve as a valuable tool in assessing the epidemiological relation between viral DNA sequences. In order to increase the likelihood of observing phylogenetic separation of sequences as well as to give strong forensic evidence regarding transmission, phylogenetic analysis needs to be performed on appropriate local control sequences and by sequencing of at least two genetic regions of reasonable length, depending on the gene under investigation. The aim of this study was to explore the suspected epidemiological linkage between DNA sequences isolated from three HIV-1 infected patients by means of phylogenetic analyses.

Phylogenetic analysis was performed on investigated sequences together with a number of local controls, that are viral sequences from infected individuals in the same location and diagnosed in a similar time period. Two genetic regions, 1.6 kb for pol and 800 bp for env, were amplified and sequenced from viral RNA extracted from plasma. Transmission clusters were assigned as those phylogenetic clades consisting of three or more sequences, fulfilling the conditions of genetic distance of 1.5% or less with posterior probability higher than 0.9 in the Bayesian analyses, for both genetic region. Maximum likelihood (ML) phylogenetic analysis was performed as implemented in Phylogenetic Analysis Using Parsimony (PAUP), using the evolutionary model selected by jModeltest software. Phylogenetic analysis revealed the presence of a single transmission cluster that accomplished all predefined sets of criteria. This cluster was composed of three viral sequences isolated from patients whose epidemiological linkage was under investigation. The mean pairwise nucleotide divergence among all observed pol sequences was 7.1% (range 0.2-12.8%) while among sequences under investigation it was 0.8% (0.3-1.1%). Regarding env sequences, nucleotide divergence among all was 16.1% (range 0.3-26.3%), while among sequences under investigation it was 1.3% (1-1.5%).

Our results strongly support the epidemiological linkage between sequences under investigation. Viral phylogenies can help to evaluate proposed epidemiological linkage and to infer the ancestral relationships of infections. However phylogenetic analysis cannot unambiguously prove that HIV-1 transmission occurred directly between two individuals, since any transmission chain may contain additional sequences not included in the analysis.

**O22**

**Antiretroviral drug resistance and viral tropism in HIV-1 CRF06_cpx infected patients failing antiretroviral (ARV) therapy**

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While the prevalence of X4-tropic viruses in subtype B is relatively well studied the distribution of tropism in CRF06_cpx (causing Estonian epidemic) is less known, especially in the treatment experienced patients with established multidrug-resistance and who are candidates for therapy with CCR5 antagonist.

Aim: to describe HIV-1 drug resistance mutations (DRMs) and co-receptor tropism in antiretroviral (ARV) treatment failing patients infected with HIV-1 CRF06_cpx and to establish their suitability to treatment with CCR5 receptor antagonists.

Altogether 12 patients were studied – all with ARV therapy failure and considered to start CCR5 antagonist therapy. Genomic viral DNA was directly sequenced in pol region and V3 loop of gp120 in triplicates. HIV-1 DRMs and tropism were detected using Stanford University Drug Resistance Database and Geno2pheno(co-receptor) 2.5. algorithm, respectively. All sequence prediction results with a false-positivity rate above 10% were considered R5-tropic.

Of 12 viruses 11 were successfully sequenced and analyzed. Patients have been diagnosed and ARV therapy initiated in 2002-2013, 8/11 cases had failure of the second ARV regimen, 4/11 of the third and in 2/11 of the fourth ARV regimen. Median viral load at the time of tropism testing was 53,326 (IQR 16,328-113,018) and median CD4+ count 184 (IQR 142-217) cells/mm³. The most commonly used regimens were EFV + 3TC plus AZT (5 cases) or plus ABC (4 cases). Of 11 viruses 10 had resistance against two ARV classes (NNRTI + NNRTI or NNRTI + INI) and 1 had triple class resistance (NNRTI + NNRTI + PI). In NRTI treated population the most common primary DRM was M184V (10/11), followed by L74V/I/L/I and K70E/R/EGK (both 4/11). In NNRTI treated population DRMs were as follows: K103N (5/11), P225H (4/411), G190A/S and K101H/E (both 3/11), others were seen in lower frequency. In PI treated patients two primary DRMs were represented – IS4V, V82A (both in same case), in INI treated population one primary DRM was represented – Y143R. The majority of viruses (10/11) were R5-tropic and all determined as CRF06_cpx by phylogenetic analysis.

The Estonian HIV epidemic has reached the stage where the first patients are considered to start treatment with CCR5 antagonists. Almost all highly resistant viruses were R5-tropic suggesting that CCR5 antagonists are an appropriate option for CRF06_cpx viruses resistant to other ARV agents.

**O23**

**The characteristics of the HIV subtype B epidemic in Slovenia**

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Slovenia is a small Central European country with a relatively modest burden of HIV disease, with fewer than 1 per 1,000 inhabitants infected. The HIV epidemic mostly affects men who have sex with men (MSM), with subtype B as the most represented subtype in over 85% of patients. The aim of this study was to establish the properties of the subtype B HIV epidemic in Slovenia up to the end of 2012.

For the purpose of this study, data and sequences were gathered from 3 previous studies conducted in Slovenia examining the prevalence of transmitted drug resistance among therapy naive HIV-1 positive patients diagnosed in the years 2000-2012. Only subtype B sequences were selected for this study (determined by the REGA HIV-1 Subtyping tool, v2.0), a total of 223 partial pol gene sequences were included, representing 52% of all patients newly diagnosed in 13 years.

The maximum likelihood (ML) phylogenetic tree was constructed using PhyML 3.0 and transmission clusters were identified according to the approximate likelihood ratio test branch support values (>0.90). The Monte Carlo Markov chain method available in the BEAST package v1.7.1 was employed, using a relaxed clock model with uncorrelated lognormal distribution and the Bayesian skyline coalescent model. The clusters previously identified in the ML and genetic analysis were reviewed and confirmed according to posterior probability values (>0.990).

Combined analysis (ML and Bayesian analysis) revealed 8 major clusters (n=10 patients), 1 group of 4 patients, 2 trios and 12 transmission pairs. Among 223 included individuals, 146 (65.5%) patients belonged to large transmission clusters comprising 10 or more individuals and 34 (15.2%) patients to small clusters of 2-4 patients, leaving only 43 (19.3%) of the Slovenian patients infected with subtype B without an epidemiological
link observed by phylogenetic inference. Statistical analysis examining the characteristics of patients found in large clusters revealed significantly fewer patients in a cluster diagnosed prior to 2005 (p=0.0388) and significantly more patients reported Slovenia as the country in which the infection occurred (p<0.0001) compared to other countries.

In conclusion, several introductions of HIV subtype B occurred in Slovenia. The majority of patients were found with a transmission link, exhibiting a closed HIV community, with the virus being transmitted predominantly between individuals within Slovenia.

Full-length genome sequences of Estonian HIV-1 CRF06 and Eastern-European subtype A1 recombinant forms
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“Eastern-European type” of HIV-1 epidemic started among Estonian intravenous drug users (IDU) population in 2000. Unlike in other former Soviet Union countries the Estonian HIV-1 epidemic was not caused by subtype A1 viruses but recombinant form CRF06_cpx and its next generation recombinants with subtype A1. A high variety of different recombinant forms has also been described in other IDU driven HIV-1 epidemics in other countries.

Aim: to sequence and describe the subtypic structure of near-full genome Estonian HIV-1 inter-subtype recombinant forms in Estonian IDU population.

The study included plasma samples from 10 HIV positive subjects collected in 2000-2010. Samples were selected based on discordant subtypes or recombinant sequences in different genomic regions in recent Estonian studies. Patients’ viral genomic RNA was reverse transcribed, amplified, cloned and Sanger sequenced in four overlapping genomic regions. Phylogenetic trees were constructed using the Maximum-Likelihood method and recombination pattern was assessed using Simplot software (similarity and bootstrapping blots). Drug resistance mutations and tropism were determined by Stanford HIV Drug Resistance Database and geno2pheno analysis tool using a false positive rate of 10%.

According to bootstrapping analysis the majority of strains (80%) indicated unique recombination structure between Estonian CRF06_cpx and Russian subtypes A1 sequences, whereas prevailing proportions of regions belong to the CRF06_cpx clade. Phylogenetic tree analysis confirmed these results indicating monophyletic clustering with Estonian CRF06_cpx or Russian subtype A1 sequences in corresponding regions. Of 10 sequences in one NMRTI DRM K103N and V179E was found and in 9 INI accessory mutations L74I was found. Of seven gag region sequences in three cases protease inhibitor associated substitution L44F, and in one case V128I, P452S and maturation inhibitor substitutions V370M were present. Of 9 env sequences one strain was R4 tropic, the others were R5 tropic. Analyzed sequences revealed high recombinational diversity of Estonian inter-subtype HIV-1 recombinant strains, which is also characteristic to other IDU HIV-1 epidemics. Nearly full-length genome sequences generated by this study provide reference material for high-throughput sequencing and for tracking the molecular epidemics in different risk groups and in Estonia and neighboring countries.

Feasibility of testing and detection of HIV-1 drug resistance in proviral DNA
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In recent years antiretroviral availability and access has become more prevalent in resource poor settings, whilst the availability of access to HIV-1 drug resistance testing remains limited and patients are often started on therapy or switched when failing without a resistance test. Proviral DNA has been proposed as a source of archived resistance mutations. We investigated the feasibility of using proviral DNA to detect previously documented plasma resistance mutations.

Amplification and sequencing of pol from proviral DNA derived from buffy coat (BC), buffy coat dried on filter paper (BCS) or dried blood spots (DBS) was performed using an in-house assay. Only 2/20 samples were amplified from long term stored buffy coat (>1 year) compared to at least one prospective sample from 10/20 patients. Six patients had a plasma viral load (PVL) <40 cp/ml at time of sampling, though 4/6 only become undetectable on the most recent sample, 2/6 had been undetectable for 149 and 819 days respectively. The remaining 6 patients had detectable PVL (median 3.1 log10 cp/ml, range: 1.7–6.2 log10 cp/ml). In contrast, 21/28 (75%) of samples which failed to amplify were <40 cp/ml, 2 had become undetectable in the most recent sample and 19 had been undetectable for a median of 577 days (range: 32–2481 days).

6/10 BCS samples showed none of the previously documented resistance for those patients, 3/10 showed some of the previously known mutations and only 1/10 showed all historic resistance, though this patient had only one documented mutation (K103N). For the BCS samples 3/4 showed none of the documented resistance, 1/4 harboured the previously known mutations (M184V, K103N). 3/6 of the DBS had none of the previously documented resistance, 2/6 showed some of the known mutations and 1/6 showed both known resistance mutations (M41L, T215S). In patients where multiple specimen types were amplified, 3/5 showed differences in mutations detected between sample types, with 2/5 correlating but having no mutations detected in any specimens. In patients with undetectable PVL, particularly those undetectable for long periods, it was difficult to sequence archived DNA. Concordance between different specimen types was variable as was concordance with previously documented mutations. Historic resistance reports remain important in the clinical management of patients on antiretroviral therapy, though proviral DNA testing may be useful in patients where historic reports are not available.

Cerebral toxoplasmosis in children and adolescents from “Dr. Victor Babeș” Hospital pediatric HIV-cohort
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Cerebral toxoplasmosis (Toxo) is rarely described in children. The Romanian pediatric cohort consists of children that have been infected parenterally in the late ‘80s. We aimed to describe the prevalence, clinical findings and outcome of Toxo in children and adolescents from the Romanian Pediatric Cohort, that have been diagnosed in the “Dr. Victor Babeș” Hospital, one of the main reference centers for HIV from Romania. Cerebral toxoplasmosis was diagnosed based on CDC case definition (presumptive and definitive diagnosis). We reviewed retrospectively the charts of all 29 children diagnosed with Toxo starting 1996, recording the demographic, HIV markers, antiretroviral treatment, clinical and neuromaging data, treatment and outcome of Toxo.

The prevalence of Toxo was 4.8% of 604 patients followed in the Hospital. Out of 29 patients diagnosed with Toxo, 19 were girls and 28 had parenterally and 1 had vertically acquired HIV. The mean age at HIV diagnosis was 11.5±6.5 years, and 15.6±5.3 years at Toxo diagnosis. In 10 patients HIV was diagnosed concomitantly with Toxo. At onset 89.7% patients had focal neurological signs and 62.1% had headache. Median CD4 count was 69 (95% CI for median 27-93) llc/mm. 28 patients had positive T. gondii IgG antibodies in plasma and/or cerebrospinal fluid. Only 6 patients had treatment with cotrimoxazole, most of them being treated with pyrimethamine/sulphadoxine combination and alternatively with atovaquone. 69% of patients had any adverse reactions to Toxo treatment. Most adverse reactions were cutaneous in 10 patients (5 severe) and anemia in 7 patients. Nine patients had antiretroviral therapy (ART) before
Toxo diagnosis, out of them 1 had mono, 1 dual therapy, 6 were failing cART and one patient had immune reconstitution syndrome. Ten patients (34.5%) died. The median survival time was 117 months. In univariate analysis survival was correlated with shorter time from onset to admission (p=0.04) while on multivariate analysis diagnosis in the post-cART period was the only factor associated with longer survival (p=0.03). 14 of 19 patients recovered with sequel, most of them motor deficits.

Cerebral toxoplasmosis in this particular pediatric cohort shared common features with that reported in adults pertaining to prevalence in pre-cART period and pathogenic mechanism. Survival was associated with a more rapid diagnosis of cerebral toxoplasmosis and with access to cART.

**O27**

Epstein-Barr virus in the cerebrospinal fluid of HIV-positive patients. Observational cross-sectional study

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Different viruses are detected in the cerebrospinal fluid (CSF) of HIV-positive patients, with controversial implications in central nervous system (CNS) impairment. Objectives: to evaluate the presence, frequency and associations of Epstein-Barr virus (EB) in the CSF in HIV-positive patients. We retrospectively analyzed CSF samples from HIV-positive adult patients (≥18 years old), with or without CNS impairment, collected between Oct 2011 and Oct 2012 in a Romanian tertiary infectious diseases hospital. We performed a multiplex PCR coupled with electrospray ionization – time-of-flight mass spectrometry (Abbott Molecular) which can simultaneously detect: herpesviruses (1-5 and 8), polyomaviruses, enteroviruses, adenoviruses and paroviruses.

The patients were characterized based on the immunological and virological HIV status, neurological findings (including neuroimaging and CSF exam) and comorbidities.

A number of 55 patients were analyzed; with a mean age of 33.4 years (31.5 median) and a male/female ratio of 1.9:1. The CD4 count had a mean of 32 (75 median and IQR=225).

The most frequently detected virus was EB in 20/55 cases. The EB-positive subgroup had a similar mean age of 33.5 years (median of 31.0) but a different male/female ratio, of 1.21. The CD4 count had a mean of 105.7 (59.5 median and IQR=156).

The following analyses refer to the EB-positive group: 17/20 patients had neurologic impairment. Imaging was performed in 15 cases and was normal in 5. CSF cellularity had a median of 2/μm, IQR=10; CSF-glucose a median of 48.0 mg/dL, IQR=34; and CSF-protein a median of 55.5mg/dL, IQR=49.5.

In 8/20 cases EB was found as singular agent in the CSF and in 12/20 it was associated with other microorganisms: other herpesviruses (3 cases), JC virus (4 cases), Mycobacterium tuberculosis (2 cases), Cryptococcus neoformans (2 cases) and Toxoplasma gondii (one case). The CSF-HIV viral load was available in 12/20 cases, being detectable in 10 cases. Regarding the neurological events (totalizing the neurological signs/symptoms, CSF exam and imaging), EB was probably causal in 4/20 cases, possibly causal in another 4/20 cases and was a bystander in 12/20 (3 cases with no impairment and 9 cases in which the impairments were strongly attributable to another germ).

EB is the most frequent agent found in the CSF (40% of HIV-positive cases), mainly in women. It can be mono-detected but it especially appears in multiple associations. In more than half of the cases EB acts as an innocent bystander.

**O28**

Evolution of progressive multifocal leukoencephalopathy in HIV-infected patients

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Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease of the CNS caused by the JC virus. It occurs in immunosuppressed individuals: patients with AIDS, malignancies, autoimmune rheumatological diseases, or those receiving immune therapy with monoclonal antibodies.

Two patients diagnosed at 13 years old with HIV infection, treated with combined active antiretroviral therapy (cART) but with curling adherence in the last years, were diagnosed after 2, respectively 3 years of stopping therapy with PML. Both patients were with a poor immunological status expressed by a low CD4 T-cell count (<50 cells/μL) and high viral load (≥427,000 copies/mL) at the moment of diagnosis. They presented headache, mild disturbances of fine movements and mild speech disorders without fever, which constantly progressed to hemiparesis, ataxia, dysarthria, aphasia, visual disturbances and swallowing disorders. The cerebrospinal fluid (CSF) was normal, the serology for Cryptococcus, Herpes simplex virus, Varicella-Zoster virus, Cytomegalovirus, Epstein Barr virus, Toxoplasma and Treponema pallidum were negative, the cultures for Mycobacterium tuberculosis, bacteria and fungi were negative. MRI scan revealed diffuse lesions in the right cerebellar hemisphere associated with emdenatous and inflammatory cortico-subcortical lesions located in the right fronto-parietal area with bilateral cerebellar extension and involvement of the pons after one month, in one patient. The other patient presented diffuse lesions located in the fronto-parietal periventricular white matter and corpus callosum. There was no mass effect. On T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences, the lesions were hyperintense. Polymerase chain reaction (PCR) for JC virus DNA in the CSF was positive for one patient and negative for the other. However, a negative PCR does not exclude this diagnosis. Under cART one patient survived with some neurological disorders, more than 5 years and today is a compliant, undetectable patient; unfortunately the other patient died after 3 months.

For both patients the diagnosis was sustained by the clinical, biological findings and neuroimaging changes on MRI, but only one was confirmed by the JC virus DNA detected in the CSF.

In such cases antiretroviral therapy should be started immediately, in order to achieve a rapid undetectable HIV viral load.

**O29**

Computerized screening tools for neurocognitive impairment in patients with HIV infection

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Neurocognitive impairment is one the non-infectious comorbidities related to HIV infection [1]. An increasing number of studies have shown the benefit of having a definite diagnosis of assessing abnormal motor, memory and cognitive functions under standardized conditions [2]. We have designed a computerized assessment tool, adapting some well-known methods of neurocognitive evaluation, and we have initiated a pilot study to assess the neurocognitive status of HIV-positive patients and controls.

We assessed patients by applying the Motor Screening Task (MST: providing data on the sensorimotor function or comprehension), the Finger Tapping Test (FTT: motor function, self-directed manual motor speed), the Symbol Digit Test (SDT: divided attention, visual scanning, tracking and motor speed), and the Stroop Task (ST: selective attention and cognitive flexibility). All subjects were evaluated with this computerized set of tests during an appointment with the clinical psychologist. For statistical assessment, the T score was used.

We assessed 10 HIV-positive patients and 15 controls. The median age and standard deviation were 26±5.11 years (range: 23-54) in the HIV group and 34±8 years (range: 25-53) in the control group. The MST scores were 720±131 ms and 629±79 ms in HIV vs. controls. The FTT scores were 167±52 ms and 163±12 ms in HIV vs. controls. The SDT scores were 664±2905 ms and 2994±681 ms in HIV vs. controls. The ST scores were 689±92 ms, 1602±1009 ms and 2045±580 ms in the HIV group and 486±118 ms, 1041±244 ms and 1023±163 ms in the control group. Despite the low number of subjects included in the study, the T score showed a statistically significant difference between the two groups for MST, SDT, ST; no statistically significant difference was observed for FTT between the two groups.
This pilot study has shown that in HIV-positive patients, the cognitive deficit tends to appear earlier than the motor one. Larger studies are needed to confirm these preliminary results and to provide more information on the clinical impact of this computerized tool for neurocognitive screening.

References

POSTER PRESENTATIONS

P1
Naïve HIV late presenters – a study for 35 months in the Infectious Diseases Hospital lași, Romania

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The HIV/AIDS Regional Center in lași follows approximately 1460 HIV-positive persons from 6 counties in the Moldova region of Romania. Objectives: The study aims to evaluate the number of late presenters in January 2011-2013. We evaluated patients admitted to the Infectious Diseases Hospital in lași, for a period of 35 months, from a virological and immunological point of view. We considered as "late presenters" naïve patients with a CD4 cell count of less than 200/cmm. From January 2011 to November 2013 there were 143 naïve patients hospitalized, of which 60 (42%) were considered late presenters, with a CD4 cell count of less than 200/cmm and a viral load of more than 10,000 copies/mL; 48 patients (80%) had a CD4<50/cmm; 14 patients died in the first 4 weeks of positive diagnosis, that is 23.3% of late presenters and 10% of all naïve patients. The median age for the late presenters was 28.4 years. However 6 patients came from the "Romanian pediatric cohort" (infected at a young age, in the early 1990’s), and were considered "slow-progressors", living with an undetected infection for 20 years. The clinical spectrum on diagnosis was: 3 cases of pregnant women detected during routine pregnancy tests; 8 patients from the men who have sex with men (MSM) population; 4 cases of pneumocystosis; 10 cases of tuberculosis; 6 patients from serodiscordant couple (infected by their HIV-positive partners); 4 patients came from other clinical services – neurosurgery, pneumology etc. We initiated pneumocystosis and TB therapy in the necessary cases, and antiretroviral therapy.

In the N-E region of our country, we still report a high number of late presenters (42% of all naïve patients), with a high mortality rate (10%). The fact that HIV-positive patients were identified in other services than the Infectious Diseases department shows a much improved collaboration between medical specialties. However, campaigns to raise awareness about the sexually transmitted diseases in vulnerable populations are still necessary.

P2
Immunizations in children exposed perinatally to HIV – from theory to practice

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Increased vulnerability of HIV infected children to numerous infections argues vaccination to protect them. Lately, we faced diseases preventable by vaccination in children perinatally exposed to HIV infection and, prematurity, abandonment, social condition, lack of understanding, drug mothers are among the causes that prevent children from immunization HIV-positive women.

During 01.01.2011-31.12.2013, in the department of immunocompromised children at the National Institute for Infectious Diseases "Prof. Dr. Matei Balș" we conducted an analysis of immunizations to 198 children exposed perinatally to HIV infection aged 0-18 months. Data from medical records and history refers to the share of vaccinations starting maternally and continuing thereafter through family physicians or pediatricians within hospital units caring for these children. A major role is parents’ avoidance to health services. Most of them rely on various reasons to avoid contact with health workers, so that most children do not benefit from prevention through vaccination. A percentage of 79.29% were vaccinated in hospital. Only 63.13% were BCG vaccinated, prematurity and knowing immunological status (CD4) representing key factors for deprivation of BCG vaccination. Optional vaccinations are hard supported by parents, such as 5.94% children were vaccinated for flu, RSV, 3.96%, 1.98% and Prevenar Rotarix. We found an increased incidence of RSV, rotavirus enterocolitis, pneumococcal pneumonia and otitis, and measles, often evolving severely.

HIV perinatally exposed infants need protection against vaccine-preventable diseases. Immunization does not influence disease progression, but the lack of vaccination can lead to severe infection, potentially fatal.

P3
Evaluation of adipose tissue changes with bioimpedance and dual-energy X-ray absorptiometry in treatment of multi-experienced HIV-infected patients

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Multi-experienced HIV-infected patients bear the burden of treatment-related toxicities over the years. This study evaluated the correlation between bioimpedance- and DXA-quantified changes of adipose tissue with duration of infection and duration of combined antiretroviral therapy (cART) in HIV-seropositive patients. A cross-sectional study, belonging to prospective grant PNCDI2 no.62077/2008, was conducted in a national reference hospital in 2011-2012. DXA whole-body adipose tissue analysis and bioimpedance analysis revealed fat and lean tissue (% and grams), android/gynoid distribution, arm+legs/trunk ratio and waist/hip ratio (WHR). There were 78 patients enrolled, including the control seronegative group. HIV-seropositive patients had equal sex distribution, median age of 33 years with mode of 20 years and body mass index of 23.6 kg/m². Duration of diagnosed infection, duration of cART and number of previous therapeutic regimens had medians of 69 months [36;113], 57 months [21;25.7], 69 months [36;113], 57 months [21;25.7], respectively. Among all variables, WHR correlated with duration of infection (rho = -0.36, p=0.05), duration of cART (rho = -0.36, p=0.05) and duration of number of therapeutic regimes (rho = -0.48, p=0.007). Also fat and lean tissue, as grams, correlated with duration of cART - rho = -0.26, p=0.048 for both. In this young treatment-experienced HIV-infected population undergoing antiretroviral therapy, the waist/hip ratio correlated best with the number of previous therapeutic regimens, inversely proportional. Adipose changes, measured by bioimpedance and DXA, were rather correlated with treatment duration than with time from diagnosis. Patients experiencing the history of antiretrovirals still present adverse effects on long term, which could influence their adherence to antiretrovirals.

P4
The prevalence of RT 245 codon polymorphisms and its association with duration of infection among HIV-1 patients in Serbia

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Amino acid (aa) substitutions at position 245 of HIV-1 reverse transcriptase (RT) have been described to be associated with the presence of human leukocyte antigen (HLA)-B*5701 allele in the host, in particular subtype B infection. Preliminary data show HLA-B*5701 prevalence of around 6.5% in Serbian population. In this study, we investigated the prevalence of RT codon 245 substitutions among HIV infected patients in Serbia. Furthermore, we analyzed the association between RT 245 aa substitutions with duration of infection, estimated by proportion of ambiguous basecalls per sequence. The study included 184 consenting, subtype B HIV infected patients aged 18 or more. The majority of patients were newly diagnosed, 150/184, while 34/184 patients were on treatment. Pol region sequences, covering protease and minimally 250 RT codons, were obtained within routine drug resistance testing. The fraction of ambiguous nucleotides in each sequence was calculated for samples drawn from naive patients. We used ambiguity percentage of 0.47% as a cut-off value delimiting recent (less than 1 year) vs. chronic infection (longer than 1 year).

In total, predominant aa at RT codon 245 was the wild type valin (V) found in 118/184 (64.1%), hence 35.9% (66/184) contained mutation at this position (among naive patients this percentage was 38% (57/150)). The most common substitution at RT codon 245 was methionine (M) 29/184 (15.7%), followed by glutamic acid (E) 20/184 (10.9%) and others. Based on the percentage of ambiguous basecalls, a total of 55.3% of naive samples (83/150) were classified as recent infection, while among these, 57.8% (48/83) had V at position 245. A total of 45.3% (68/150) were classified as chronic infection, with the presence of V at RT codon 245 found in 69.1% (47/68). We did not find statistically significant association between polymorphisms at codon 245 and duration of infection (p=0.208).

The frequency of RT 245 substitution found in our study exceeds the estimated prevalence HLA-B*5701 in Swedish population. This may be related to the presence of other, similar HLA alleles, limiting significance of the correlation between HLA-B*5701 and RT codon 245 variation. Furthermore, no statistically significant difference was found in the prevalence of RT 245 substitutions between recent and chronic infection. This finding could point to the possibility of a HLA induced selective imprint, during viral evolution in an infected patient.

P5
Characteristics of Kaposi sarcoma in HIV-infected patients
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Objective: to describe clinical and laboratory characteristics; to assess predictors for death in HIV-infected patients with Kaposi sarcoma (KS).

We performed a retrospective study of HIV-infected patients diagnosed with KS in one infectious diseases hospital in Romania, between January 2008–November 2013. KS diagnosis was established on physical examination, skin biopsy, and for visceral involvement upper gastrointestinal endoscopy, bronchoscopy and computed tomography. KS was staged according to the AIDS Clinical Trials Group (ACTG) [1] and the Mitsuysu classification system [2].

We identified 27 HIV-infected patients with KS. The median age was 42 years (IQR 34–52) and 18 (67%) were male. The median CD4 count at HIV diagnosis was 195 cells/cmm (IQR 55–313), while at KS diagnosis the median CD4 count was 101 cells/cmm (IQR 41–270). Eighteen (67%) patients had a CD4 count <200 cells/cmm. The median HIV viral load at the time of KS diagnosis was 120,000 copies/ml (IQR 316–328,322). HIV infection was diagnosed before KS in 19 patients (70%), with a median time of 6 months before KS diagnosis of 7 months (IQR 0–58). The most frequent KS localization was the lower limb in 16 (59%) patients and 7 (26%) patients had disseminated KS. Oral, gastrointestinal and pulmonary involvements were seen in 10 (37%), 4 (15%) and 3 (11%) patients respectively. Concomitant opportunistic infections were diagnosed in 20 (74%), while other malignancies in 3 (12%) patients. According to the ACTG classification 16 (59%) patients had poor risk KS. Fifteen (50%), 6 (22%), 1 (4%) and 5 (18%) were in stage 1, 2, 3 and 4, respectively according to the Mitsuysu classification. Six (22%) patients received specific KS treatment: three local radiotherapy and three systemic therapy (two with interferon; one with liposomal doxorubicin).

The overall mortality was 41% with a median duration between KS diagnosis and death of 6 months (IQR 2–15). Gastrointestinal involvement (p=0.019), poor-risk KS in ACTG classification (p<0.001) and stage IV Mitsuysu (p=0.006) were associated with death in univariate analysis.

The mortality rate in this study was high, due to poor immunological status, extended KS and high incidence of opportunistic infections, but also due to the lack of specific systemic treatment.

References

P6
Epidemiologic patterns in HIV infection in Mureș county
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Despite the important scientific progress regarding HIV pandemics registered during the last decade, more and more cases of HIV infection are diagnosed every year, as HIV testing practices vary across Europe. Purpose: to identify epidemiologic trends in newly diagnosed patients with HIV infection in the center of Romania. Method: we performed a retrospective, cross-sectional study, over a 5-year period (January 2009 – December 2013), upon all new cases of HIV infection, diagnosed in Mureș county. We analyzed demographic data, transmission patterns, level of CD4 T-lymphocytes and patients’ outcome. Over a 5-years period, we have diagnosed 58 new cases of HIV infection, 63.79% male / 36.21% female. Average age was 27 years, median – 23 years, with extremes between 2 and 55 years. Most cases came from urban areas (65.38%). Transmission patterns included risk groups: men who have sex with men (MSM) – 4 patients, unknown multiple partners – 3 patients, HIV-infected sexual partner – 15 patients, screening at delivery – 4 patients, 1 case of mother-to-child transmission. The dominant pattern was heterosexual transmission – 27 patients. CD4 T-cells count registered an average level of 349 cells/μl, median 335 cells/μl, ranging from 2 to 1304 cells/μl, 23 (39.65%) patients were late presenters. We registered 3 deaths (5.17%). While previous epidemiologic data from our region suggested an unknown route of transmission in children born around the 1990’s, during the last years, the dominant epidemiologic pattern in HIV infection in Mureș county was heterosexual transmission. An important category of newly diagnosed patients was represented by late presenters, with potential unfavorable evolution. We registered a concerning trend of sexual transmission of HIV infection in serodiscordant couples, despite medical education.

P7
Late presenters (LP) in the last 3 years in the anti-AIDS center of Cluj, Romania
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Objectives. In Europe 50% are late presenters (LP). In a previous study we showed that between 2000-2010 LP represented two thirds of cases and the main transmission route was sexually, with 5% in men who have sex with men (MSM). We proposed to analyze the epidemiologic, clinic and therapeutic issues of late presenters in the last three years and to compare with the previous study. Our center is monitoring about 330 HIV patients.
We performed a retrospective study of the medical records of 113 HIV newly infected adults, admitted in the Infectious Disease Clinic of Cluj between 01.01.2011-30.06.2013. The patients were divided in two samples: sample I as LP and sample II with CD4 counts more than 350/cmm. Fisher’s exact test was used for statistical analysis: p<0.05 was considered significant.

There were 64 patients (56%) LP and 49 (44%) in sample II. The average age was 37/34 years, sexually transmitted in 56/48, MSM 16/18, (33% MSM in LP), males 43/42, urban area 50/44, symptomatic HIV testing 51/15, life-threatening conditions 24/1, deceased 8/0. We found statistically significant values in the LP for: HIV testing as symptomatic patient (p<0.0001), clinical life-threatening conditions (p=0.0001), rate of deaths (p<0.005); in the sample II we found significant values for HIV testing as screening (p=0.01) and HIV test request (p=0.0009). In the last 3 years there was no significant difference between the two groups: MSM transmission, concordant/discordant couples or celibate, provenience area, age more than 40. No significant values for LP between 2000-2010 and 2011-2013 (p=0.1), but differences in MSM transmission in the last 3 years (p=0.0002).

Between 2000-2013 LP were 56-66% with influence on mortality rate. In the last 3 years the transmission rate on MSM is increasing from 5% to 33%. We have no intravenous drug users. HIV testing with informed consent delays the diagnosis and represents a barrier for earlier HIV testing.

**P8**

Epidemiological aspects of HIV infection in the Republic of Moldova

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HIV infection in the Republic of Moldova continues to represent a major problem of public health, which is kept under constant surveillance and monitoring. On January 1, 2014 the cumulative number of persons identified with HIV was 8,588 people, representing a prevalence of 166.74 cases per population of 100,000. In 2013, HIV incidence was 17.18 cases per 100,000 population. Cumulative AIDS was diagnosed in 2,464 persons (28.7% of people diagnosed HIV positive). 1,752 people died at the onset of the epidemic (20.5% of all people diagnosed with HIV).

The HIV epidemic in the country is characterized by three periods with some features:

- 1987-1995 registering sporadic cases in some areas, mainly among foreign students - sexually transmitted ways;
- 1996-2001 expanding geographic areas and spreading predominantly among injecting drug users (IDU), the route of transmission through injecting drug use;
- 2002-present spreading in all administrative territories, including in rural areas, increasing the number of persons infected sexually, increasing the percentage of impaired women.

The incidence of HIV in Moldova increased significantly since 2003. So far, the epidemic has affected most intravenous drug users (IDU), commercial sex workers (CSW), men who have sex with men (MSM) and their partners, thus being classified as epidemic outbreak concentrated in population groups with high risk of infection. The country is assured access to preventive services to all population groups, especially IDU, CSW and MSM. It is also ensured access to treatment, care and support for HIV infected persons and AIDS patients.

**P9**

Changes in HIV transmission profile in Arad county

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Initially HIV infection in Arad County was impacting infant population. Later most of the new cases were adults, but even so trends in recent years are moving in the same way for adults and children, the latter being infected through vertical transmission.

The hypothesis was to determine the relationship between age of cases at diagnosis moment and route of transmission in more than two decades from 1990 till now. We have used data from the medical records of HIV-AIDS department of Arad County Emergency Hospital, from 1990 to 2013 statistical processing with SPSS 14.0 for Windows, MedCalc and Epi Info Analysis.

Of the 437 patients, children and young people 1-19 years were 68%, gender ratio M/F being 1.31. Parenteral route of transmission covered 47%, sexual 22%, vertical 2%, and unknown for 29% (statistically significant relationship between age at diagnosis and transmission path p=0.000). Only 149 patients are monitored /34/, 174/40% are out of records and 114/26% died. There are many associated infections like HBV, HCV, TB, CMV, ITS, total 166/38% among total of 437 cases. Relative risk for parenteral transmission was 2.34. In the first decade compared to the second one and reached up to 7.7 for sexual transmission route in the second decade, compared to the first decade.

Pediatric HIV infection versus adult HIV infection rate is changing from 5.53 in the first decade to 0.35 in the second one, risks of sexually transmitted infection becoming dominant for the second decade.

**P10**

Evaluation of anthropometric and virologic data in newborn from HIV positive mothers

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Constanţa used to be one of the most affected counties of Romania by HIV in children. Nowadays in Constanţa there are an increasing number of HIV positive young women at fertile age who have babies. Even though there were implemented active measures for prevention of mother to child HIV transmission we still diagnose mothers with HIV after delivery. On the other hand HIV infection increases the risk of intrauterine growth restriction (IUGR) of newborn.

The objectives of this study were to evaluate the proportion of children born from HIV positive women who presented IUGR; and to evaluate materno-fetal transmission rate of HIV in Constanţa County.

We performed a retrospective study on the relevant parameters in newborns and mothers: demographic data; CD4 count and HIV viral load in last trimester of pregnancy of mothers; HIV viral load in newborn. We analyzed anthropometric data of the newborn: weight, length, cranial circumference, and Apgar score. Statistical analysis was performed using SPSS version 19.

Over a period of 6 years and 2 months, 135 newborn from 117 HIV+ mothers have been monitored. From all 135 children born from HIV positive mothers 5 were HIV positive. The median age in mothers was 23 and mean 23.08 (range: 17 to 39, SD=3.58). The mean Apgar score in newborns was 8.47 (range: 2 to 10, SD=1.022), and median 9. The mean birth weight in newborns was 2692 g (range: 1000 to 3900, SD=516.389), and median 2700 g. The proportion of children with birth weight less than 10th percentile was 58.05%. The mean length was 47.66 cm (range: 39 to 52, SD = 2.75), with a proportion of children below the 10th percentile of 27.4%. Infants who presented below the 10th percentile for weight and length were 23%. About 21.48% of infants were below the 10th percentile for weight, length and cranial circumference. Mean CD4 count in mothers in third trimester of pregnancy was 415.14 (range 27-1156), and median 397. 53.3% of mothers were with HIV viral load undetectable in the last trimester of pregnancy. In the studied period the mortality rate was 6.7% in children and 5.9% in mothers.

The materno-fetal rate of HIV transmission was 3.7%. More than half (58.05%) of the infants born to HIV positive mothers were small for gestational age. 23% of infants were with IUGR and 23% of them presented symmetrical IUGR.
Mother-to-child transmission of human immunodeficiency virus (HIV) infection decreased in the last years due to the implementation of: HIV testing, antiretroviral (ARV) medications, delivery by cesarean section and discouraging breastfeeding. In Romania, pregnant women could acquire HIV infection as adults or could have a long history of disease and ARV treatment (ART), belonging at the Romanian cohort.

Aim: to evaluate the risk factors for HIV transmission from mother-to-child during pregnancy and delivery.

Retrospective study based on patients’ electronic medical records files and AIDS database (Cluj and Mureș AIDS Center) of all children born by HIV+ patients at the detection and ART prophylaxis. Statistical analysis was performed with chi square test and multiple regression.

54 newborns were born by 45 HIV infected women during the study period, 8 (14.81%) of them being diagnosed with HIV infection. The women’s average age was 23.82 (min 18, max 38), 29 women belonged to the Romanian cohort. The AIDS stage was: A for 12 patients, B for 19 patients and C for 23 patients. 6 out of 45 women (13.33%) didn’t receive ART during pregnancy, being diagnosed during labor. Plasma viral load during pregnancy was determined for 36 women: undetectable for 8 women, less than 400 copies/mL for 5 women and more than 400 copies/mL for 23 patients. Delivery was with elective cesarean section for 47 newborns (87.03%), infant ART prophylaxis was administered in 48 newborns (88.88%). The risk of mother-to-child HIV transmission was significantly lower with: ART during pregnancy (<0.001) not important of ARV association, cesarean section (p=0.001) and infants’ ART prophylaxis (p=0.03).

The risk of mother-to-child HIV infection is high in Romania; the percent of women not tested for HIV infection during pregnancy is low; the risk of HIV infection transmission was significantly lowered by ART during pregnancy and in infant, as prophylaxis, and by elective cesarean section.

P12 Impact of HIV-1 infection on mortality among new diagnosed cases in a hospital in Bucharest
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According to new published data, HIV/AIDS infection currently knows an increase of 8% for the countries of Eastern Europe and Central Asia. This happened in our country too, where a new way to get have started HIV: appeared: intravenous drugs used of so-called soft, legal drugs (ethnobotanicals) near the classic heroin. Objectives: To study the impact of HIV infection and the trend in mortality in a cohort of 497 newly diagnosed patients enrolled between 01.01.2011 and 31.12.2013 in the Clinical Hospital of Infectious and Tropical Diseases “Dr. Victor Babes”, Department Casa Andreae, Bucharest. These new cases were intravenous drug users (IVDUs) but also late and very late presenters sexually infected and nonIVDUs.

We performed a retrospective study of patients newly diagnosed with HIV infection that died during the 36 analyzed months. The research was based on clinical records and autopsy reports. Patients lost from follow up or died at home were excluded. Our cohort enrolled 497 patients: 249 IVDUs and 248 nonIVDUs. Men were in greater proportion, dominated the IVDU group. The average patient age was 30.8 years old, similar age for both genders. Sixty-eight (13.65%) patients died. 17 IVDU and 41 nonIVDU (total deaths were 106 - 20.1%) those diagnosed before 2011 but who died in the analyzed period were excluded). Most deaths were recorded in IVDU in 2012, and in nonIVDU in 2011. Mean CD4 cell count was 126.62 lymphocytes/cmm in IVDU and 75.75/cmm in nonIVDU. IVDUs were classified in approximately equal proportions in C3/B3 class and the other category in class C3. HCV co infection was present in all IVDU and only in 7.31% of nonIVDUs.

IVDUs causes of death in descending order were MSSA sepsis and tricuspid endocarditis (in 2013 began appearing MRSA) followed by pulmonary and disseminated tuberculosis (TB), HCV decompensated cirrhosis and drugs overdoses. In nonIVDUs, opportunistic infections were causes of death (toxoplasmosis, PCP, neglected TB treatment, lymphoma). Death occurred at a mean of 14.5 weeks (limit 3 days-104 weeks) for nonIVDU and 17.7 weeks for the IVDU weeks (range: 1 day- 93 weeks) for IVDUs.

P13 Brief intervention to strengthen adherence to ART in prison
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We have learned that the HIV+ prisoners in antiretroviral therapy (ART), frequently discontinue their treatment. That is why we build up and deliver a brief intervention, to see if we can increase their adherence to treatment. We are presenting now the results one month after the intervention, those at 3 month will be available at the congress time.

In the prison hospital Jilava near Bucharest are held the inmates who are HIV+, their number is around 280 and 178 are in treatment. We delivered to 180 of them in series of 30 inmates a 30 minutes session consisting in a short presentation on HIV and the importance of treatment in obtaining undetectable viral loads and then a Q and A session. All of the inmates had access to a written material with almost the same message as the presentation. We than analyze and compare the adherence to treatment in the month before the intervention and the month after the intervention by counting the refused dosages as treatment is delivered strictly supervised by the nurses. We plan to analyze the attrition of the intervention with follow-up at 3 months and 6 months.

As the inmates come and go into the Prison Hospital, we have retained in the analysis only 150 patients that have received the intervention, comparing them with a lot of 50 that didn’t, all of them being convicted for at least another year. 120 patients were in ART and 30 were not. In the comparing group 30 were in ART. The demographics of the 2 groups were similar. In the month before the intervention there were 41 refused doses (from 230) and 2 refusals for initiation of therapy. In the comparing group there were 9 refused doses from 55. After the intervention we had less refusals in both groups.

As the adherence was improved after the brief intervention, even though there were positive results in the comparing group that received only the written material, we agreed to deliver the intervention to all the inmates that are HIV positive. The results at 3 months will be available at the National HIV Congress time.

P14 Characteristic of HIV/AIDS infected patients at the detection and HAART initiation
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We evaluated the clinical features, immunological and virological indices in HIV/AIDS–infected patients at the detection and antiretroviral therapy (HAART) initiation.

We followed up 149 adult patients diagnosed with HIV/AIDS infection between the years 1997-2011 and supervised in the specialized department of the Clinical Hospital of Infectious Diseases “Toma Gheorghiţa”. These patients received HAART since 2011. The late diagnosis is defined by the presence of AIDS associated diseases and/or the level of CD4 <350 cells/µL.

Studying general features of HIV infection depending on specific laboratory indices of this disease, was found that nearly two-thirds (63.09%) of patients with HIV/AIDS are detected late and more than half
of them (59, 57%) have already advanced HIV infection which develop specific clinical manifestations of HIV/AIDS such as oropharyngeal candidiasis, tuberculosis and wasting syndrome, which represents a strong correlation between disorders of the immune system activity expressed by the considerable decrease in CD4 levels and facilitation to develop the opportunistic infections. The predominant route of HIV transmission was heterosexual in 87.25% of cases, and IDU in 12.75% cases. In particular deserves attention IDU transmission path, which is prevalent among men and 89.47% compared with 10.53% in women (p<0.05). Very important is the fact that men more frequently than women are diagnosed with concomitant diseases (viral hepatitis, respiratory, digestive diseases). Thus, one quarter of men with HIV/AIDS (25%) were diagnosed with viral hepatitis versus only 13.08% of women (p<0.05) at both detection and at the initiation of HAART. AIDS was diagnosed in 44.97% of cases on detection and on initiation of HAART AIDS had almost already three quarters of studied patients (73.83%). At HAART initiation, advanced HIV infection (CD4 <200 cells/µL) showed about two-thirds (62.42%) of patients compared with 37.58% at CD4 counts between 350 and 201 cells/µL (p<0.01). This study showed that more than half (63.09%) of HIV/AIDS-infected patients were detected late, with the number of T-lymphocytes CD4 <350 cells/µL, with or without AIDS related conditions, which determine necessity to improve HIV testing strategies.

P15
The impact of infectious diseases on personality traits - comparative study on HIV versus hepatitis B and C
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Personality traits are in constant dynamics and they are influenced by significant events in the life of the person. The study aims to evaluate chronic infectious diseases patients (HIV, HBV, HCV positive) from a psychological perspective, for a period of 9 months, January-September 2013. We evaluated 52 HIV-positive patients in evidence at the Iași Regional Center, and 48 patients diagnosed with chronic hepatitis B or C. They were evaluated using the A. P. Questionnaire to detect accentuated personalities, developed by Dr. H. Schmieschek.

Most patients enrolled were female (51%). The median age was 24.3 years for the HIV-positive lot and 34 for the HBV/HCV lot; 34% of them came from rural areas. Average schooling level was 10 classes; 38% came from broken families or foster care; 15.3% of the HIV/AIDS patients and 62.5% of HBV/HCV patients had a stable job. All of the HIV positive patients were in active therapy, polyexperimented. All of the HBV/HCV infected patients were in active therapy with pegylated-interferon. The A. P. Questionnaire found in HIV infected patients: 90% emotivity, 85% anxiety, and 65% dysthymia (alternative episodes of exaltation and depression). In the case of HBV and HCV infected patients, 60% scored high anxiety, and 65% dysthymia (alternative episodes of exaltation and depression). In the case of HBV/HCV infected patients, 60% scored high anxiety, and 65% dysthymia (alternative episodes of exaltation and depression).

The dominant personality traits that are accentuated when faced with an infectious disease have certain specific trends depending on the disease, duration of therapy and psycho-social impact of the diagnosis.

P16
Epidermodysplasia verruciformis in a HIV patient – case report
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Epidermodysplasia verruciformis (EV) is a rare genodermatosis with an autosomal recessive pattern, characterized by an unique susceptibility to chronic cutaneous infections involving specific human papilloma virus (HPV) types in the genus β. Acquired EV, with clinical features similar to those in congenital EV, occurs only in immunocompromised patients, including those with HIV, lymphoma, transplant recipients and patients undergoing immunosuppressive therapy.

Patients frequently present with verruca plana-like lesions (discrete or confluent, often red-brown papules) distributed on the extremities, usually dorsal hands, face and neck. Other characteristic clinical findings include flat scaly pinkish, red-brown or hypopigmented guttate macules or thin plaques, which are similar to pityriasis versicolor, especially if they develop on the trunk. EV is considered a premalignant condition and almost half of the patients develop in the fourth and fifth decades squamous cell carcinoma, most commonly on sun-exposed area.

We report the case of a 26 years-old female patient with a history of HIV infection since the age of 6 years, receiving antiretroviral therapy, with a CD4 lymphocyte count of 545/µL and undetectable viral load, who presented for treatment of asymptomatic but cosmically distressing skin lesions that had been present for almost 10 years.

Dermatological examination revealed isolated flat and some confluent, reddish-brown discrete papules and erythematous macules, 2-7 mm in diameter, distributed on the dorsal hands, forearms and knees. Dermoscopy exhibited well circumscribed erythematous area with a whitish, scaly surface. Histopathology showed hyperkeratosis, slightly thickened epidermis, enlarged keratinocytes, some with basophilic and others with eosinophil cytoplasm, hypertrophic nuclei, perinuclear halos, and intracytoplasmic keratohyalin granules.

The diagnosis of EV verruca plana-like was confirmed. The patient was counseled about the disease and topical therapy with imiquimod cream was initiated, without improvement at one month follow-up. The patient is still on treatment and further therapeutic options are considered (cryotherapy, TCA peeling, electrotherapy and acitretin).

EV in HIV is a rare condition, with only 30 cases reported in medical literature, and this patient is the first case of EV-HIV coinfection in our HIV department.

P17
HIV-associated Burkitt lymphoma with bone marrow and cerebral invasion in a patient with history of Plasmodium falciparum infection
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HIV infected patients are more likely to develop non-Hodgkin lymphoma (NHL). Burkitt lymphoma (BL) is a highly aggressive NHL, associated with immunosuppression, especially with HIV. According to WHO classification there are three clinical types of BL: endemic, sporadic and immunosuppression-associated. Sporadic lymphoma was described especially in children (40% of child lymphomas in USA and EU). Two cofactors seem to be associated with BL: Epstein Barr virus (EBV) and Plasmodium falciparum (PF) infection. PF and EBV are well-known co-factors in the pathogenesis of BL, but the mechanisms of interaction remain unclear.

We present a 51 year-old male, who developed lymphadenopathy, prolonged fever, weight loss, splenomegaly and seizure. The patient was admitted to a Hematology University Hospital. After lymph node biopsy he was diagnosed with BL. A specimen of bone marrow from the right iliac crest showed gross invasion by Burkitt tumor cells.

The patient tested positive for HIV and he was referred to the National Institute of Infectious Diseases “Prof. Dr. Matiei Balș”, Bucharest. According to CDC Classification System for HIV Infection the patient had AIDS (C3 stage with a CD4 count of 39/cmm) and a high HIV viral load (500,262 copies/mL). The patient’s medical history revealed Plasmodium falciparum malaria 4 years ago, while he was living in South America. Epidemiological data revealed more than 200 sexual partners in the last two years. At admission to our hospital he had pancytopenia: white blood cells 1400/cmm, with 600 neutrophils and 600 lymphocytes, hemoglobin 9.6 g/dL and platelet count 25,000/cmm. The patient was tested for EBV infection and high titer of anti- VCA antibodies was found. ART was initiated with TDF-FTC-lopinavir/rr with good virological outcome (after 6 weeks of therapy the viral load was 383 copies/mL). Cerebral MRI showed diffuse lymphomatous invasion. After
3 weeks of ART the patient was referred to Hematology Hospital where chemotherapy was started. Post-chemotherapy the pancytopenia was more severe: white blood cells – 200/cmm with CD4 count – 10/cmm, platelets – 15,000/cmm and hemoglobin – 7.9 g/dL. The BL response after chemotherapy was poor and the patient died two months after the diagnosis, despite the good virological outcome.

We present a rare case of NHL in a HIV-infected patient, with multiple co-factors for BL: HIV infection, EBV infection and *Plasmodium falciparum* infection. The prognostic in AIDS depends on the comorbidities’ outcome.

**P18**

Liver damage in HIV+HBV co-infected patients determined by transient elastography

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In our country the prevalence of HIV-HBV co-infection in young infected patients, between 1985-1990, transmitted through nosocomial or vertical path is approximately 40%.

We followed the prevalence and risk factors associated with liver damage in HIV+HBV infected patients. Longitudinal evaluation of liver fibrosis was carried out in the patients included in the study group, by transient elastography (TE). Several studies using non-invasive methods for the assessment of fibrosis have been performed in HIV infected patients, and in patients co-infected with hepatitis virus B, although up to now these methods have not been validated for this segment of the population. For statistical analysis, the TE results were designated to different stages of fibrosis in accordance with the previous recommendations. The predefined cut-off values were: F0-F1 ≤7.1 kPa, F2-F3 >7.1 and ≤12.5 kPa and for cirrhosis (corresponding to F4) >12.5 kPa.

We included in the study 71 patients co-infected with HIV and hepatitis B. 71.85% of patients had minimal liver damage, 18.30% of them had moderate to severe fibrosis, 9.85% were F4. Patients were divided according to CD4 count into three groups: CD4 (0-200/cmm), (200-500)/cmm, and >500 cells/cmm. By applying the ANOVA test we found significant differences between the 3 groups (p=0.037<α=0.05, F=3.472) and reading the Bonferroni table shows that there are significant differences between the values of FibroScan only in patients coinfected with HIV+HBV with CD4 appropriate intervals (< 200 and >500) and for cirrhosis (corresponding to F4) >12.5 kPa.

We divided the patients into two groups: HBV-DNA level >400 copies/mL in 52 patients and ≤400 copies/mL in 19 patients. The most common causes of chronic diarrhea in patients with AIDS are infectious enteritis (with CMV or *Cryptosporidium*), *Clostridium difficile*-associated diarrhea was observed in 5 cases (15.62%) and two patients (6.25%) were diagnosed with *Mycobacterium avium* complex infection. Four patients (12.5%) were diagnosed with inflammatory bowel diseases – 3 cases with ulcerative colitis and one patient with Crohn’s disease. For two patients (6.25%) the diagnosis was ascendant colonic adenocarcinoma and one patient (3.12%) was diagnosed with terminal ileum lymphoma. In 3 cases (9.37%) the final diagnosis was “AIDS enteropathy” (an enteric pathogen was not detected). However, there was a striking correlation between the severity of gastrointestinal diseases and the CD4 lymphocyte count.

Most common causes of chronic diarrhea in patients with AIDS are infectious enteritis (with CMV or *Cryptosporidium*) and *C. difficile*-associated diarrhea. Survival and outcomes are linked to severity of immunodeficiency.

**P20**

Chronic diarrhea in patients with acquired immunodeficiency syndrome (AIDS)

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Chronic diarrhea, defined as two or more loose or watery stools per day for at least 1 month is common in patients with AIDS. It’s a causal relationship between the immunosuppression and the diarrhea in these patients. We evaluated the most common causes of diarrhea in patients with AIDS.

32 consecutive patients with AIDS were submitted with chronic diarrhea (19 males, 13 females), mean age 20.82±8.97 years. Generally, the same work up as for a patient without AIDS should be initiated: previous or recent history (including a review of the patient’s drugs), physical exam, blood tests, stool examination and abdominal ultrasonography were performed for all patients. Abdominal plain films, stool culture, total colonoscopy, upper digestive CT (computed tomography) scanning or MRCP (magnetic resonance cholangiopancreatography) were done in selective cases.

Fifteen of the cases (46.87%) were with infectious enteritis (Cytomegalovirus or *Cryptosporidium*), *C. difficile*-associated diarrhea was observed in 5 cases (15.62%) and two patients (6.25%) were diagnosed with *Mycobacterium avium* complex infection. Four patients (12.5%) were diagnosed with inflammatory bowel diseases – 3 cases with ulcerative colitis and one patient with Crohn’s disease. For two patients (6.25%) the diagnosis was ascendant colonic adenocarcinoma and one patient (3.12%) was diagnosed with terminal ileum lymphoma. In 3 cases (9.37%) the final diagnosis was “AIDS enteropathy” (an enteric pathogen was not detected). However, there was a striking correlation between the severity of gastrointestinal diseases and the CD4 lymphocyte count.

Survival and outcomes are linked to severity of immunodeficiency.
Patients with HIV may present with both TB and PCP and in these patients, TB seems to account for the most serious symptoms of their disease that require hospitalization. We report the case of a 36-years old patient admitted in our department in 23 October 2013, for persistent fever, headache, oral candidiasis, productive cough, weight loss and severe asthma. He tested positive for HIV with a CD4 of 7 cells/µL and a viral load of 930,795 copies/mL. In the blood culture we isolated Hafnia alvei and the chest CT scan showed "a ground-glass aspect" suggestive for a Pneumocystis carinii pneumonia (PCP). The pneumological evaluation established the imagistic diagnostic of miliary tuberculosis and recommended treatment with tuberculostatic drugs and antibiotic.

Severe sepsis has emerged as a common cause of hospital admission for those living with HIV/AIDS. Sepsis patients had significantly higher in-hospital mortality than did nonsepsis patients. Clinicians should be aware that patients with HIV/AIDS may present with concurrent pulmonary TB and PCP, especially in regions that are hyperendemic for TB.

**P22**

**Hepatitis C cell culture system – a valuable tool for understanding viral resistance mechanisms**

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Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV) co-infect five million people worldwide. HIV/HCV co-infection represents the major cause of liver related morbidity among the HIV infected patients. The current HCV standard of care consisting of pegylated α-interferon and ribavirin has variable efficacy and considerable side-effects. A major step towards a more efficient and better tolerated therapy has been done by the recent approval of the first direct acting antivirals (DAAs) to enter the clinic. Moreover, there are numerous DAAs which are advanced in clinical trials targeting different steps in the viral life cycle. Due to the variety and efficacy of HCV drugs in the clinic or in the pipeline, there is hope for an interferon free treatment. However, despite the increased efficacy of DAAs with or without interferon and ribavirin, viral resistance still represents an issue. Thus, phenotyping resistance "in vitro" should help the clinician to better personalize the HCV treatment. HCV drug resistance phenotyping has become possible due to the HCV cell culture system. HCV cell culture (HCVcc) system relies on the JFH-1 strain of genotype 2a which is able to replicate in cell culture without adaptive mutations. HCVcc system allows the analysis of every step in the viral life cycle: replication, secretion and infectivity. Clinically relevant chimeric viruses are available covering different HCV genotypes. This allows the "in vitro" evaluation of the viral fitness starting from patient derived viral sequences. We are presenting the complementarity between drug resistance genotyping and HCVcc system in understanding the mechanisms of HCV drug resistance. The use of a drug resistance phenotyping assay for clinical purpose will be discussed.

**P23**

**Incidence and clinical forms of tuberculosis in HIV infected adults: 2013 versus 2007**

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Tuberculosis (TB), yet an endemic disease in Romania with a high prevalence compared to the average European incidence, had a slight descendent curve. But in the last 3 years we noticed a new phenomenon: an epidemic of tuberculosis among newly HIV infected intravenous drug users (IVDU). Objective: to determine the incidence, clinical and epidemiological characteristics of the new TB cases and TB reactivation in two different years, 2007 and 2013 (before and after HIV epidemic in IVDU) in our clinic of HIV infected adults.

We found a higher incidence of new infected TB cases or TB reactivation in 2013 (45 cases) versus 22 cases in 2007. The average age of patients was lower (33.6 years) in 2013 than in 2007 (35.6). Predominance of male patients was higher in 2013 (79%) vs. 76% in 2007. HIV transmission in 2013: 61% IVDU, 35% sexual transmission, 2% horizontal transmission cohort; in 2007 74% sexually transmitted infection, 14% horizontal infections. In 2013, 41% of HIV-TB coinfected patients were romani ethnics (81% of them IVDU) versus 5% in 2007.

The localization of TB infection was comparable in 2013/2007: disseminated TB 46% vs. 51%, pulmonary TB 51% vs. 50%, peripheral adenopathy 1 case each year. In 2007 we had 47% patients with sensibility to the 2 major first class drugs – hydrazine (H) and rifampin (R), resistance to H 6%, to R 12%, MDR 6%. In 2013 we have 85% patients HR-sensitive, 3% H-resistant, 3% R-resistant and 10% MDR.

The global mortality of the two groups of patients was higher in 2007 than in 2013 (32% vs. 23%). Deaths related to TB infection were higher in 2013 than in 2007 (89% vs. 57%). Many cases of TB in IVDU HIV infected patients were severe: (58% disseminated TB). Mortality among HIV-TB coinfected IVDU was 50%, versus 8% in non-IVDU patients. TB had a high prevalence in HIV patients, in 2013 as in 2007, involving significant mortality and morbidity. A lot of newly HIV infected persons are still late and very late presenters. We are expecting that the epidemic of ethnotubercular drugs will raise the prevalence of TB. New techniques of TB antibiotic can reduce mortality.

**P24**

**Epidemiology of HIV/AIDS infected persons in the western part of Romania in 2013**

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HIV transmission continues in Romania, despite decades of concerned efforts to inform the public about HIV and its consequences and reduce individual risk behaviors. This is a retrospective study carried out in 2013 in the western part of Romania, in the counties Arad, Caraş-Severin, Hunedoara and Timiş. In 2013 there are 846 patients with HIV/AIDS in active evidence, 86.4% in combined antiretroviral therapy (cART). Despite intense counseling, 30 (4.1%) patients interrupted willingly their antiretroviral therapy. There are 93 new infected persons in 2013, mostly men who have sex with men (MSM). 10 children were born in 2013 from HIV infected mothers, 1 was diagnosed while pregnant, 1 at delivery, 8 were known with HIV/AIDS prior to delivery. All 10 newborns received prophylaxis with antiretrovirals for 6 weeks. 11 (1.33%) patients were diagnosed with tuberculosis, 10 with pulmonary tuberculosis and 1 with tuberculous meningoencephalitis. HIV/AIDS infection remains an important public health problem in the Western part of Romania.

**P25**

**Investigation on anti-cangliosides antibodies in asymptomatic HIV patients**

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Anticangliosides antibodies were observed in neoplastic diseases, bacterial and viral infections, autoimmune diseases and neurological disorders. Objective: assessment of anticangliosides antibodies anti-βG1, -βG2, -GM3, -GD1a, -GD1b, -GT1b, -GQ1b of IgG type in asymptomatic HIV patients. The study was based on the prospective analysis of 32 patients with asymptomatic HIV infection, with no retroviral treatment, without altered neurological status associated with the disease and 48 healthy subjects. Anticangliosides antibodies were determined by immunoblot method, using Euroline kits.
In healthy subjects, antigangliosides antibodies of IgG type against all the mentioned gangliosides were negative.

In patients with HIV infection, antigangliosides antibodies of IgG type had the following frequency: 6.2% anti-GM1, 15.7% anti-GM2, 12.5% anti-GM3, 18.7% anti-GD1a, 6.2% anti-GD1b, 9.4% anti-GT1b, 18.7% anti-GQ1b. The statistical analysis showed a significant difference between anti-GM2, anti-GD1a and anti-GQ1b status in HIV group compared with the control group.

The authors considered that gangliosides expressed on the membrane of HIV infected cells induced antigangliosides antibodies’ synthesis. Antigangliosides antibodies’ presence seems to be a primary immunological event in HIV infection and might play a physiopathological role in the studied viral infection.

**P26**

Extrapulmonary tuberculosis in HIV infected patients from the cohort of “Dr. Victor Babes” Hospital, Bucharest, Romania

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The infection with *Mycobacterium tuberculosis* remains the most frequent opportunistic infection in HIV seropositive patients. In Romania the incidence of tuberculosis (TB) in general population is the highest in Europe with 70.9 per 10,000 inhabitants.

We investigated the incidence of extrapulmonary tuberculosis in “Dr. Victor Babes” Hospital cohort and its epidemiological, clinical and outcome particularities.

We performed an observational retrospective study during 2003-2013 among the HIV infected patients from our cohort. We selected the patients with extrapulmonary tuberculosis. The data was obtained from the medical charts and outpatient records.

From 280 cases of confirmed infection we found 55 cases of extrapulmonary tuberculosis. The transmission route was parenteral in 72.55% (95%CI 58.75 to 87.40) of cases. The median age at TB diagnosis was 24 years (95%, CI 20.16 to 25.03) with male/female ratio of 1.21. At the time of TB diagnosis the median CD4 count was 87 cells/cmm (95% CI 72.67 to 131.31). The percent of patients with concomitant pulmonary and extrapulmonary localization was 57.7% (95% CI 40.79 to 72.78). The number of patients with recurrent TB was 17 and 5 had more than one extrapulmonary TB in the studied period. The most frequent extrapulmonary involvement was ganglionar 35/51 (69.7% 95% CI 54.91 to 79.74). The commonest manifestations were fever (57.5% 95% CI 40.79 to 72.78), weight loss (30% 95% CI 17.25 to 47.46) and adenopathy (24.2% 95% CI 12.60 to 41.25) and the median time from the onset to diagnosis was 4 weeks (95% CI 2.611 to 5.209). In 54.5% (95% CI 40.79 to 72.78) of the cases the smear was positive, cultures were positive in 69.7% (95% CI 55.61 to 85.10) and in 30% (95% CI 17.25 to 47.46) of cases was made the diagnosis by histopathologic examination. In 45.5% (95% CI 32.50 to 64.78) we obtained an antibiogram that confirmed MDR TB in 11.5% (95% CI 2.37 to 24.34). All patients received treatment and 7.84% (95% CI 6.17 to 31.40) abandoned treatment and 11.76% (95% CI 2.37 to 23.4) died.

Although the extrapulmonary involvement is not very frequent, the diagnosis can be challenging and can take a lot of time especially when it is difficult to obtain a specimen. In a febrile immunodefpressed patient extrapulmonary TB should be always considered.

**P27**

Avascular osteonecrosis mechanism – between osteoporosis and antiphospholipid syndrome

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HIV infected patients receiving antiretroviral therapy (ART) can develop avascular osteonecrosis, 45 times greater than the general population.

Avascular osteonecrosis increased in the last few years in patients with HIV infection. The most important mechanisms for avascular osteonecrosis in HIV-infected patients are: changes in bone metabolism, especially osteoporosis correlated with protease inhibitors and coagulopathy and antiphospholipid syndrome, frequently described in HIV infection. Aim: to describe different mechanisms of avascular osteonecrosis

We present two HIV-infected patients under antiretroviral therapy who developed avascular osteonecrosis. First patient, male, 38 year-old, with AIDS-C5, with good immuno-virological outcome under AZT-3TC and lopinavir/ritonavir, developed severe osteoporosis after 5 years of ART, diagnosed by DXA test with a T-score < -2.5. The patient had: C4-C5-C6 severe osteoporosis with high fracture risk, with segmental instrumentation applied at those levels, and then bilateral avascular necrosis of femoral head (ANFH) with bilateral hip arthroplasty. ART regimen was changed and the patient received 3TC-ABC and Nevirapine. The patient didn’t have other risk factors for avascular osteonecrosis or osteoporosis: nonsmoker, normal CD4, undetectable viral load, without dyslipidemia. Despite ART changes, the patient developed bilateral osteonecrosis of the right knee and of both humeral heads.

The second patient, male, 23 year-old with HIV-B3, was treated in 2007 with AZT-3TC and lopinavir/ritonavir. After 9 months of ART the patient had normal CD4 count and undetectable viral load but developed right ANFH as stage II, diagnosed by MRI, without surgery recommendation. DXA didn’t show signs of osteoporosis or osteoasenia. The ART regimen was changed and the patient received 3TC-ABC and raltegravir with good ANFH outcome. After one year the patient discontinued the ART. One year later symptoms related with avascular osteonecrosis reappeared and bilateral ANFH was diagnosed by MRI. The patient had low CD4 count (<200/cmm), high HIV viral load and positive antiphospholipid antibodies. The patient had risk factors for coagulopathies: smoker, recreational drug use, alcohol consumer, uncontrolled HIV infection with low CD4. We restated the same regimen with 3TC-ABC and raltegravir with a good outcome for bone affliction. When HIV infection was well-controlled, the antiphospholipid antibodies became negative and bone affliction was improved.

We emphasize the importance of metabolic disturbances in HIV-infected patients, among them avascular osteonecrosis with different mechanisms. Both, ART and uncontrolled HIV infection can affect bone metabolism and vascularization.

**P28**

Comorbidities in HIV infected patients admitted to County Infectious Diseases Hospital Tg-Mureş in 2013

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The prevalence and incidence of comorbidities in HIV-infected patients has varied over the past 30 years, depending on the studied population. The purpose of this paper is to review the various conditions registered in HIV-positive patients admitted to the 1st Infectious Diseases Clinic of Tg-Mureş.

We performed a retrospective cross-sectional study, on 124 HIV infected patients (average age 27 years, 49 female, 85 subjects in AIDS stage), admitted to the HIV Department of the 1st Infectious Diseases Clinic of Tg-Mureş during January – December 2013 (253 hospitalizations, overall 2,415 days, median hospital stay 7 days). Co-infections (viral hepatitis, tuberculosis, bacterial, fungal, parasitic and other viral conditions), as well as pluri-organic comorbidities were noted and correlated to gender, level of immune-deficiency, history of HIV infection, adherence to antiretroviral therapy and outcome. Statistical analysis was performed with Mann-Whitney non parametric test.

Patients had an average of 6 comorbidities such as: 98 various bacterial, viral, fungal and parasitic infections, 91 hematologic disorders, 83 metabolic disorders, 77 gastrointestinal conditions, 68 acute respiratory disease cases, 43 neurological issues, 39 mental health problems, 35 hepatitis B infection, 32 chronic respiratory diseases, 25 cases of tuberculosis, 24 bone disorders, 12 cardiovascular diseases, 5 sexually transmitted diseases, and 2 malignancies. We registered statistically significant differences regarding the presence of comorbid conditions and gender (male>female, p=0.003), immune status (more comorbidities in
Background

Cryptococcosis represents a major life-threatening fungal infection in patients with severe HIV infection. Cryptococcal meningoencephalitis is the most common manifestation of cryptococcosis in patients with advanced immunosuppression. Objectives: evaluating risk factors for severe evolution of patients with HIV infection and meningitis.

Possible risk factors were analyzed in 33 HIV-infected patients with meningitis, of the 2,100 patients monitored for HIV infection in the National Institute for Infectious Diseases "Prof. Dr. Matei Balș" during 2011-2013.

Epidemiological data, CD4 serum and glycyrhachia values were collected from patient records. Etiological diagnosis was made by direct microscopic examination, stained smears microscopy, India ink test, cryptococcus antigen identification by latex agglutination and culture, identification and antifungal susceptibility testing were performed with Vitek 2C analyzer.

Cerebrospinal fluid glucose was 33 mg/dL in the 7 alive patients and 23.6 mg/dL in the 5 deceased. All samples having positive latex, had India Ink positive. Only three samples showed no growth in culture. The analyzed patients were infected with subtype F1 HIV-1 viruses, as indicated by subtyping analysis. All the patients had antiretroviral (ARV) therapy interrupted at the moment of cryptococcal meningitis diagnosis. As expected, resistance mutations were not present in PR and RT genes, with few exceptions such as K103N, E138A.

The cryptococcal meningitis is very rare among Romanian HIV-1 infected patients, frequently associated with advanced immune suppression, lack of ARV therapy and other comorbidities (TB and HBV infection).

P29

Risk factors in HIV/AIDS patients with cryptococcal meningitis

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The treatment of extra pulmonary tuberculosis in HIV infected patients experienced to antiretroviral therapy raises major issues of adherence, drug interactions, side effects and limited antiretroviral alternatives. The case is a 24 year old woman from countryside, mostly probably infected in 1989. She was diagnosed with HIV infection in 2000 after repeated admissions in hospital for pneumonia. She started ART when diagnosed with a favorable evolution: CD4 cell count increased from 200 to 674 cells/cmm, and HIV RNA levels became undetectable. She turned 18 in 2008 and refused to take her treatment for almost two years. She returned to the hospital in April 2010 with a CD4 cell count of 140 cells/cmm. She started again antiretroviral therapy with ABC+3TC+FPV/r. In April 2013 she is admitted with night sweats, chills and fever. At that time her CD4 cell count was 144 cells/cmm and had 461,000 copies/mL RNA-HIV. Her chest XR showed right pleural effusion, widened mediastinum and the CT revealed infiltrative-like lesion at subcarinal and retrocarinal level. Biopsy was performed and she was diagnosed with ganglionary tuberculosis. She started anti-TB treatment HRZE 7/7 and the ART was changed to ABC+RAL+T20.

The anti-TB regimen is changed after three months to rifampicin and isoniazid 7/7 because she accused arthralgias, tingling of the extremities, blurred vision and decreased visual acuity. She was diagnosed with hyperuricemia (pyrazinamide) and optic and peripheral neuritis (ethambutol).

New visit at the clinic for fatigability, after 7 months of antiretiroviral therapy with ABV+RAL+T20. The CD4 cell count was 9 cells/cmm and RNA-HIV was 61,000 copies/mL. She admits taking 1 cp of Raltegravir BID, but denies any other adherence problem. The resistance test showed evidence of resistance to some NRTIs, to all NNRTIs, to RIL and to no resistance to PIs. The tropism test showed that maraviroc can be used.

We have excluded relapse of tuberculosis and other diseases associated. The ART was changed again to TDF+DRV+LMV and the anti-TB treatment is change to isoniazid and moxi-floxacin.

Adherence can be an important issue when treating patients for long periods of time. Other important issues are the drug-drug interactions (rifampicin – PIs) and the increased side effects which may lead to loss of good friends (Raltegravir). The poor outcome for this patient may be due to poor HIV and tuberculosis control.

P31

The multiple faces of tuberculosis in HIV infected patients – a continuous challenge

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Tuberculosis (TB)/HIV co-infection represents a major problem in many regions of the world, including Romania. TB is a leading cause of death among people infected with HIV and HIV infection is the most important risk factor for progression from latent to active TB. TB can occur at any stage of HIV disease and its manifestations depend on the severity of immunosuppression. The proportion of extra-pulmonary tuberculosis in HIV infected patients has increased. Aim: to analyze the cases of pulmonary and extra-pulmonary TB in HIV-seropositive patients monitored in Third Department of the "Matei Balș" Institute.

We performed a retrospective analysis of all HIV infected patients monitored in our clinic from 2000 to 2014 in order to establish the location of TB, the diagnosis methods, the correlation with the immune status and the outcome.

122 patients were retrospectively analyzed; from them, 18 patients were diagnosed with certain, probable or possible TB infection (14.75%). Sex ratio in TB group was M:F=1.57:1 and mean age was 39.7 years old at the moment of TB diagnosis. TB occurs at a variable level of immunosuppression (CD4 count from 6 to 460/cmm) - 4 patients (22.2%) in stage 2 - CD4=200-500/cmm and 14 patients (77.8%) in stage 3 - CD4<200/cmm. Mean CD4 count in TB group was 113.23/cmm vs. 218.33 in non-TB group. Pleuro-pulmonary TB accounted for only 27.7% of all cases - one pleural effusion and 4 pulmonary TB. In most of cases, TB infection was extrapulmonary (72.3%): 5 cases of lymph node TB (11.11%) and 3 cases with unknown location (7.27%). Mean nadir CD4 count in non-TB group. Pleuro-pulmonary TB accounted for only 27.7% of all cases - one pleural effusion and 4 pulmonary TB. In most of cases, TB infection was extrapulmonary (72.3%): 5 cases of meningoencephalitis (27.7%), 3 cases of disseminated TB (16.66%), 2 cases of lymph node TB (11.11%) and 3 cases with unknown location (16.66%). TB was microbiologically confirmed in only 6 cases – 33.33% by blood culture, 2 by PCR (one from CSF and one from pleural effusion) and 1 by histopathologic exam (lymph node biopsy). In 9 cases TB was probable but without bacteriologic confirmation and in 3 cases TB was possible – prolonged fever with a good outcome under anti-TB medication. Quantiferon TB was performed in only 8 cases – in 6 cases was positive, in one case was negative and in one case was
undetermined. Three patients died: one patient because of disseminated TB and two patients because of other HIV-related comorbidities. TB can occur in any stage of HIV infection. Microbiological diagnosis in TB is positive in a small number of cases.

P32
Metabolic complications during HIV-treatment with protease inhibitors in patients from Brașov

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Objective: to evaluate the effects of treatment with protease inhibitors on serum level of triglycerides, cholesterol and glyceremia in HIV-infected patients, in assessing the need of monitoring patients.

We performed a retrospective study on 25 patients with HIV infection, in evidence of the Infectious Diseases Hospital of Brașov, treated with protease inhibitors in the treatment regimen. We studied the levels of cholesterol, serum triglycerides and blood glucose at the beginning and during treatment with protease inhibitors.

We found increases in serum cholesterol levels in 72% of patients and in 83.33% of them were increasing by 50% from baseline; growth exceeded baseline in 44.45% of cases. Serum triglycerides have increased to 68% of patients, with up to 100% from baseline in 64.5% of cases and in the rest of the patients the increase was marked, beyond 100% exceeded normal values in 64.5% of cases. Blood glucose was maintained at normal levels in 56% patients and increased in 24% of cases.

Treatment with protease inhibitors is associated frequently with increased serum levels of cholesterol and triglycerides; hyperglycemia has rarely occurred. Patients treated with protease inhibitors require rigorous monitoring of the metabolism of fats and carbohydrates in order to establish appropriate treatment for early complications that may have occurred.

P33
The risk for developing neurological sufferances in Romanian HIV infected patients – predictive criteria

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Objective: to establish a set of predictive criteria for the occurrence of neurological sufferances in a group of Romanian HIV infected patients (Px).

Retrospective study (January 1990 – January 2011): we have stratified data (CD4 count, HIV-RNA level, total duration of antiretroviral treatment (ART) and duration of a certain ART regimen) from 98 Px diagnosed with neurological sufferances. Chi2 test, odds ratio (OR), relative risk (RR) and Receiver-Operator-Curve (ROC) have been used for statistical reasons. OR increases exponentially with the decrease of CD4 count (max. 37.68), total ART duration (max. 17.7) and duration of a certain regimen (max. 62.37) and linearly with the HIV-RNA level (max. 47.75). RR increases linearly for all the studied parameters (7.36, 3.73, 2.88 and 7.64 respectively). ROC analysis suggests that, for our group of Px, less than 178 CD4 cells/cmm (sensitivity = 58.2, specificity = 85.2, p<0.0001), more than 20,750 HIV-RNA copies/cmm (sensitivity = 72.2, specificity = 46.7, p value not statistically significant), a total ART duration of less than 41 months (sensitivity = 49.0, specificity = 77.6, p<0.0001) or less than 23.5 months for a specific ART regimen (sensitivity = 72.4, specificity = 63.2, p<0.0001) should be predictive for neurological sufferances.

CD4 count, HIV-RNA level, total ART duration and duration of a certain ART regimen could be used to predict the occurrence of neurological sufferances in Romanian HIV infected Px, however the best results (given the ROC sensitivity and specificity) are provided by the duration of a specific ART regimen.

P34
PML - not a surprise in four young HIV infected patients

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An important cause of mortality in patients from Romanian cohort remains progressive multifocal leukoencephalopathy (PML) caused by the polyomavirus, JC virus (JCV).

PML is an opportunistic infection and one of the AIDS-defining conditions in HIV-infected patients and is associated with both HIV-1 and HIV-2. We perform a retrospective study in which we included 4 patients from Cluj-Napoca HIV Center. These patients belong to Romanian cohort and were with poor adherence to treatment.

We collected information on clinical and immunological status, microbiological and virological analysis, neuroimaging, treatment and outcome.

From 4 patients with a median age of 20.75 years at the moment of PML diagnosis, 3 were male and 1 was a female; 3 died and 1 is alive. All patients were already in stage AIDS C3 at the moment of PML diagnosis and with a CD4 lymphocytes level below 20 cells/cmm.

The onset was insidious in all cases with focal neurological signs (hemiparesis, facial palsy, dysarthria and mental alteration) without fever. In two cases we performed lumbar puncture that revealed clear CSF, with normal level of glucose and proteins, negative Gram stain and negative culture but with JC virus load positive (RT-PCR JCV from CSF).

The imagistic methods (cerebral MRI) showed in all cases lesions localized in white matter, without mass effect from these lesions. For two cases we completed examination with cerebral MR spectroscopy which revealed spectroscopic disorders specific for PML.

In all cases we excluded other etiologies by serological, bacteriological and imagistic tests.

All patients received cART with good penetration in CSF and corticotherapy, but in 3 cases neurologic disorders evolved to tetraparesis, aphasia and profound altered mental status and finally death.

1 patient had a good neurologic recovery and remains with easy ataxia and dysarthria.

In these cases PML is a result of low adherence to treatment of patients from Romanian cohort and opportunistic infection was not a surprise. The most important differential diagnosis was HIV encephalopathy.

We can conclude that our patients with PML had a poor prognosis despite intensive cART with good penetration in CSF.

P35
Prevalence of hypertension (HT) among HIV infected patients from Galați

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With over 300 HIV infected patients, Galați is the fourth area of HIV prevalence, the majority is nosocomially infected being now young adults with old infection. Objectives: to determine the prevalence of hypertension (HT) and to compare the results with national references provided by SEPHAR study.

162 HIV positive patients 45% men, 55% women, usually assessed in Outpatient Clinic, aged from 20-54 years (mean 26 years) were included in this cross-sectional study. Data about blood pressure (BP, total and HDL-cholesterol CD4, weight, height, smoking were collected from patient dossier and compared with general population data. HT was defined according to ESC/ESH 2013 guidelines as systolic BP>140 mmHg or diastolic BP >90 mmHg. Statistical analysis: MedCalc. Men usually systolic BP (SBP) of HIV patients is 110±11.4 mmHg vs. 136±22.6 mmHg (p<0.0001). HT prevalence is 8% vs. 40% (p=0.0398) more frequent in HIV positive men (61.5%) than HIV positive women (38.5%). Abnormal total cholesterol is 32% vs. 26% (p=0.4407), HDL-cholesterol <55 mg%
prevalence is 77% vs. 13% (p<0.0001). Smoking prevalence among HIV patients is 54.6% vs. 29% (p<0.0001) more frequent among men than women. Obesity by BMI is 1.23% for BMI>30, 15.4% for BMI 25-29. Mean CD4 is 698 cells/cm³. No correlation between CD4 levels and HT was made.

1. Overall HT appears to be rare among HIV population due probably to high prevalence of young age therefore further observation is required to establish the real prevalence among HIV patients. Men appear to be more affected by HT than women.
2. Dyslipidemia is more frequent among HIV patients than general population, low HDL-cholesterol prevalence is statistically significant higher than general population, as marker for chronic HIV infection.
3. There is no explanation for significant higher prevalence of smokers among HIV-infected patients than general population; male gender is more affected than female gender.
4. Obesity by BMI is unusual among HIV patients due probably to young age and ongoing chronic infection.
5. In conclusion longitudinal study is needed for a better description of hypertension and cardiovascular risk factors among this special population.

P36

Difficulties in the management of the meningitis with C. neoformans
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The management of the meningitis with C. neoformans raises many problems: the choosing of the appropriate antifungal therapy, the prevention and/or the control of the complications, the correct management of the antiretroviral therapy.

We report two cases with HIV infection same immunological and clinical stage, the first of them with relatively recent infection, the second with long-term infection (>20 years) and antiretroviral therapy - experienced, but discontinued for 4 years, who developed the same opportunistic infection: cryptococcal meningitis.

Although immunological status was similar in both patients, cerebrospinal fluid inflammatory response was stronger in patient infected latest; both had increased cerebrospinal fluid pressure, requiring repeated lumbar punctures.

The antifungal treatment algorithm was applied according to guidelines, to availability of medications at that time and antifungal susceptibility testing results.

Although the combination of fluconazole plus flucytosine is known as being clinically inferior to amphotericin B-based therapy, faster rate of cerebrospinal fluid sterilization was seen in patient with greater cerebrospinal fluid inflammatory response rather than in patient receiving antifungal therapy considered as “gold standard”.

To avoiding the immune reconstitution syndrome, antiretroviral therapy was initiated in both cases after more than 4 weeks of therapy of opportunistic infection (after 2 weeks of sterilizing cerebrospinal fluid cultures); however, the patient with long-term HIV infection developed immune reconstitution syndrome after 21 days of initiating therapy.

Choosing antiretroviral therapy was achieved in both cases according to guidelines, depending on the patient’s medical history (including previous regimens therapy) and drug interactions.

Our cases illustrate that the same disease can have different solutions because the patient makes the difference.

P37

Assessment of neurocognitive impairment in HIV-infected patients from the Regional Center Mureș
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Neurocognitive assessment in HIV-infected patients in Regional Center Mureș was held between 01.01.2013-31.12.2013 on a group of 26 patients. Out of the 26 patients recruited and evaluated, all were included in the national database and 6 patients were recommended for comprehensive assessment at the “Victor Babeș” Hospital - Bucharest. Inclusion criteria: patients born between 1987-1991, at least 8 years of education, who had not been institutionalized, without psychiatric conditions.

We used the following methods for neurocognitive screening of patients included in our study: International HIV Dementia Scale, Simioni questionnaire, Beck Depression Inventory, Patient’s Assessment of Own Functioning Inventory (PAOFI).

Preliminary psychological evaluation in 26 patients showed no evidence of neurocognitive deficit. Out of the 6 patients who underwent comprehensive neurocognitive testing, 1 patient was diagnosed with neurocognitive deficit, obtaining lower values than the group’s average for most tested areas.

It is necessary to validate a tool to identify the neurocognitive changes caused by HIV. The final results will be given by the National Screening Program.

P38

Two cases of HIVAN in young AIDS patients
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HIV associated nephropathy (HIVAN) is a quite frequent pathology among HIV infected patients with a high incidence in black people. Among the 800 patients from Western Romania, infected with HIV type 1, mostly subtype F, none were diagnosed based on renal biopsy with HIVAN until 2010, albeit several renal abnormalities have been described among HIV patients based on a complex etiology.

We present two cases, both Caucasian, a 25 years old female and a 26 years old male, HIV infected in the early 1990’s with horizontal transmission. First case was diagnosed with HIV infection as late-presenter and staged C3 at the age of 10 when she was admitted in coma secondary to toxoplasmic encephalitis. The first manifestations of nephropathy were detected 6 years later with decreased creatinine clearance. The second case was HIV diagnosed at the age of 19, in 2007, during hospital admission for acute glomerulonephritis with secondary renal impairment, as a late-presenter staged also C3. The patient presented hepatitis B co-infection as well as chronic CMV infection. Renal biopsy was performed on both patients and the revealed aspects of focal and segmental glomerulosclerosis, applicable for HIVAN. Both patients started HAART immediately after diagnosis, none of the medications used had been showed to induce renal impairment and both of them had creatinine clearance adjusted dosing of antiretroviral (ARV) treatment, but in spite of similar ARV and supportive treatment, the two cases had different outcome. One had a very slow rate of decrease in renal function while the second one (similar to literature data) had a rapid evolution towards chronic kidney disease, within 3 years dialysis had to be initiated.

Compliance to antiretroviral treatment improves survival rate globally (with presumable late onset for chronic kidney disease). Renal biopsy remains the standard in order to diagnose HIVAN. As far as patients are aging with AIDS, renal manifestations may become more frequent and a comprehensive oversight is needed.

P39

Latero-cervical lymph node tuberculosis and brachial herpes zoster in a patient diagnosed with HIV infection
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Latero-cervical lymph node tuberculosis and brachial herpes zoster in a patient diagnosed with HIV infection
Tuberculosis and Herpes Zoster are known as common opportunistic infections in patients diagnosed with HIV infection. This is the presentation of a clinical case with right latero-cervical lymph node tuberculosis associated with brachial Herpes Zoster and oral candidiasis in a patient recently diagnosed with HIV infection, stage C3.

The authors present the case of a 23 years old student, admitted in the Clinic of Infectious Diseases Timișoara for a latero-cervical lymphadenopathy in the right side, that appeared simultaneously with a progressively asthenic syndrome associated with weight loss in the past three months, night sweats and loss of appetite. We mention that she presented a maculo-papular and vesicular rash in the upper limb, accompanied by burning pain. In order to establish the diagnosis, multiple biological samples were collected (blood cell identification, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), lingual swabs, throat swabs, blood culture, ELISA test for HIV Ab, Western blot test, CD4 lymphocyte, viral load, etc.) and paraclinical investigations (lymph node biopsy, histological examination and cultures for Koch bacilli; cultures for Koch bacilli in the secretions from the bronchial lavage; chest radiography).

From the biological samples we highlight: WBC=3,240/µL, ESR=125 mm/1h, CRP=32.83 mg/L, fibrinogen=3.77 mg%, HIV Ag-Ab=positive, HIV test positive: viral load>200 000 copies/mL, there were no radiological changes in the lungs. The histopathological exam of the lymph node biopsy pleaded for lymph node tuberculosis. The cultures for Koch bacilli in the secretions from the bronchial lavage were positive. The culture for Koch bacilli in the lymph node biopsy was also positive. The lingual swab, using Sabouraud medium culture revealed Candida albicans. Putting together the clinical data and the biological samples and the test results, we have established the diagnosis of lymph node tuberculosis, brachial herpes zoster, oral candidiasis, HIV infection stage C3. Under treatment with antituberculous and antiretroviral drugs the evolution of the patient was favorable.

The early diagnosis of the opportunistic infections allows the detection of the patients with HIV infection and the establishment of a specific and efficient therapy.

**P40**

**Issues in cytomegalovirus chronic infection in HIV patients**

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**BMC Infectious Diseases 2014, 14(Suppl 4):P40**

The prevalence of cytomegalovirus (CMV) in HIV infected patients is 90%. Both CMV and HIV are involved in the pathogenesis of metabolic and cardiovascular diseases.

The study retrospectively evaluated the correlation of CMV infection with lipodystrophy (LD) and hypertension (HTA) in HIV patients who have been beneficiaries of medical care in Galați, during 2013. The evolution of anthropometric parameters, CDC-HIV categories, the immunity by LyCd4, the category of detectable or undetectable HIV-RNA, the categories high/low for values of cholesterol, triglycerides, glucose, fibrinogen and for serum creatinine (Scr) were compared with the groups of patients with LD, HTA and normal BMI. The results show a lower lymphocyte count in patients with LD, HTA, and normal BMI compared to the controls. The immune system is more affected by CMV infection in patients with LD, HTA and normal BMI compared to the controls.

**P41**

**Disseminated toxoplasmosis in an HIV positive patient in CART era**

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Toxoplasmosis is a disease caused by the intracellular parasite Toxoplasma gondii. Toxoplasmosis is considered one of the most common cerebral opportunistic infections in HIV/AIDS patients. It develops when CD4 count falls below 100 cells/µm², either from acute exposure to the parasite or from reactivation of latent infection. These patients may also develop extra-cerebral toxoplasmosis such as ocular toxoplasmosis and pulmonary diseases. Another clinical manifestation described in HIV-infected patients is disseminated toxoplasmosis which consists of fever, pulmonary infiltrates and sepsis-like syndrome.

We present a case of a 22 years old female patient diagnosed with HIV since her childhood. Over the years she was uncompliant to combined antiretroviral therapy (cART). After 16 years from her HIV diagnosis she presented an acute hepatitis type C with severe prolonged evolution, from which she slowly recover after a period of 3 months. After discharge she was well for about one month but came back with left hemiparesis difficulties in speech and visual disturbances. Also during this last hospitalization she presented a severe bronchopneumonia. After 20 days of hospitalization she died. Postmortem histopathological examinations revealed a disseminated toxoplasmosis involving multiple organ systems: central nervous system, lung, liver, spleen and lymph nodes. Lung examinations revealed bronchopneumonia due to multiple opportunistic infections with T. gondii, CMV and fungal infection. We noticed also an extensive ulcerated esophagitis of HSV and fungal etiology.

In immunosuppressed patients disseminated toxoplasmosis has a polymorphic clinical presentation requiring a more attentive investigation because it may hide also an involvement with other opportunistic infections. The syndrome of disseminated toxoplasmosis is affecting more than two organs and it is highly lethal in HIV positive patients.

**P42**

**Challenges in treating HIV-infected patient with disseminated Kaposi’s sarcoma and military TB**

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Kaposi’s Sarcoma (KS) is the most common malignancy in HIV-infected patients. It’s induced by an infection with the Human Herpesvirus 8. AIDS-related Kaposi sarcoma tends to have an aggressive clinical course because it may involve all skin, membranes, lymph nodes, stomach, gut, lung or liver. A 32-year-old patient was diagnosed in 2009 with HIV infection and disseminated KS. Purple macules and nodules were disseminated on the trunk, limbs and lingual mucosa. He was a late presenter with CD4-T cell count 30 cells/µL and 108,000 copies/mL HIV-RNA. With antiretroviral therapy (ART) the clinical, virological and immunological evolution were very good: the CD4-T cell count increased to 156 cells/µL and the viral load was undetectable. Unfortunately, he became non adherent, and after 2 years of absence he returned in very bad condition with pericarditis, pleurisy, ascites and a low CD4-T cell count (13 cells/µL). The changes showed by the chest CT scan, the results of pleural biopsy, the clinical findings raised the suspicion of disseminated KS and miliary tuberculosis. Despite all the treatments (Mega-ART, antituberculosis chemotherapy, opportunistic infections prophylaxis): the pericarditis and pleural fluid was always recovered. Weekly thoracentesis were needed and CD-4 T cell number had not increased as we expected (the maximal value was 88 cells/µL) although the viremia was undetectable.

There are 5 years since our patient was diagnosed with HIV infection and disseminated KS. In front of a patient with HIV-infection and symptomatic visceral or pulmonary KS, regardless the viral load, cytotoxic chemotherapy is recommended after the immunological status is improved. Another option is thoracoscopic talc pleurodesis which has been reported extremely effective in the malignant pleural effusion.
P43 Oppotunistic infections and immune reconstitution inflammatory syndrome (IRIS) in HIV infected patient – late presenter in cART era: case report

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HIV-infected individuals are at high risk of developing numerous opportunistic infections. The severity of these infections may increase proportional to the immunosuppression degree. We must pay special attention to immune reconstitution inflammatory syndrome (IRIS) in order to prevent worsening symptoms and death. HIV coinfection is associated with high mortality rate despite effective antiretroviral therapy.

We present the case of a 42 male patient who was diagnosed with AIDS and pulmonary tuberculosis in 2011 in our clinic. Our theme includes clinical, biological, immunological, virological evolution and therapeutics of this patient.

He was a late-presenter patient with advanced immunodepression at baseline: low CD4 count, increased viral load in blood and cerebrospinal fluid. After a month of tuberculosis treatment, antiretroviral therapy was instituted according to guidelines. During one year the patient subsequently developed IRIS and, one by one, several opportunistic infections, including CNS involvement.

Thus he presented: Cryptococcus neoformans meningoecephalitis resistant to fluconazole with multiple relapses, TB meningoecephalitis, severe form of CMV disease with encephalitis, demyelinating lesions, necrotic ulcerative stomatitis and esophagitis with HSV, systemic candidiasis, severe bacterial infections with multidrug-resistant germs.

Diagnoses were based on the usual investigations, including molecular biology techniques (RT-PCR: Mycobacterium tuberculosis, JC Virus, Cryptococcus neoformans), viral resistance testing, PLEX-ID, MRL. Viral PLEX-ID identified the presence of Epstein Barr virus in CSF at a high level.

Opportunistic infections occurred imposed specific therapy and reconsideration of antiretroviral therapy with CNS penetration ARV (score Leitendre). The patient was adherent to ARV therapy. The evolution was initially favorable under specific therapy with clinical, immunological and virological improvement. Unfortunately, about 6 months after diagnosis, the patient developed CNS lymphoma possibly in relationship with increased levels of Epstein Barr virus in CSF, having fatal outcome.

The evolution of this case pointed out once again that in a patient with AIDS at the time of initiating ART, it should be considered the possibility of IRIS and future opportunistic infections, associated with a poor prognosis. Therefore it is important to detect persons with HIV infection in the early stages of the disease in order to obtain a favorable evolution.

P44 Helicobacter pylori – HIV co-infection and dyspepsia

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Helicobacter pylori infection is one of the most frequent causes of dyspepsia in the general population. As gastrointestinal symptoms are a common complaint among HIV-positive persons, the purpose of the present study is to assess the role of Helicobacter pylori infection in this category of patients.

We performed a retrospective, case-control study on two groups of HIV-infected patients admitted to the Infectious Diseases Clinic I, Tîrgu-Mureș and healthy for Helicobacter pylori infection by stool antigen detection: group A – 36 dyspeptic subjects and group B – 5 patients without dyspeptic complaints. We compared the two groups from the point of view of the frequency of Helicobacter pylori infection. Statistical analysis of data was performed with the help of GraphPad programme.

4 (11.11%) HIV-positive patients with dyspeptic symptoms tested positive for Helicobacter pylori infection, while none of the patients in group B was diagnosed with Helicobacter pylori infection (p=1.0000, OR=1.523).

Although none of the asymptomatic patients in our study was diagnosed with Helicobacter pylori, the absence of a statistically significant association between Helicobacter pylori infection and dyspepsia among HIV-positive patients may suggest that other etiologies should be searched in HIV-infected patients with gastro-intestinal complaints.

P45 Relative risks for digestive and respiratory episodes in patients with HIV co-infection

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HBV, CMV or TB co-infection worsen progression of HIV, due to specific pathogenicity of etiologic agents and antimicrobial therapy which is required to be initiated.

Authors have tried to establish a link between HBV, CMV or TB co-infection and the risks for emergence of digestive and respiratory episodes. We have used data from the medical records of HIV-AIDS department of Arad County Emergency Hospital for HIV patients in evidence in 2013. Data were analyzed by SPSS 14.0 for Windows, MedCalc and Epi Info Analysis.

Of the 149 patients 38 presented HBV, CMV or TB co-infection (25.5%) and statistically was significant in the history of their recorded adverse reactions that changing ART regimens was required (P=0.0324), they also displayed digestive and respiratory episodes P=0.0057 and P=0.0033, being at relative risk of 1.7344 to 1.6692 respectively for these episodes compared with HIV patients.

HIV patients with co-infection stand at increased risk for digestive and respiratory intercurrent infectious episodes, monitoring them being a basic element for their quality of life and for survival rates improvements.

P46 Favorable outcome of pregnancy on antiretroviral treatment in a patient with HIV-infection

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Antiretroviral (ARV) therapy in pregnant women is particularly important for both patients and for her future child. Objectives: To present clinical and biological evolution of pregnant patients under ARV therapy combination Combivir+Kalera (CBV+kAL) with good adherence to treatment.

The authors present the case of a patient, 22 years old, from urban area, monitored in Infectious Diseases Clinic Tîrgu Mureș in 2010 with HIV infection stage C2. Personal pathologic history: oropharyngeal candidiasis, toxoplasmosis, suppressive otics, bilateral coxofemoral and knee arthritis, HIV encephalopathy depressive disorder, hypotrophy weight, static encephalopathy, dyslipidemia, chronic HIV hepatitis. Biochemistry, bacteriology and immunology were performed in the hospital laboratory using an automatic biochemical analyzer (Konelab 301) and an automated system VITEK 2 Compact. Assessment of viral load by PCR was performed in the Laboratory of the National Institute for Infectious Diseases "Prof. Dr. Matei Balș", Bucharest. Throughout pregnancy the patient received ARV treatment with CBV+kAL.

Results: the beginning of pregnancy: Hb=13.1 g%, H=4,270,000/cmm, Tr=285,000/cmm, L=6,000/cmm, ESR=32 mm/1h, fibrinogen=3.6 mg%, ALT=42 U/L, AST=31 U/L, cholesterol=200 mg%, triglyceride=156 mg%, glycemia=102 mg%, ASLO=200 U/L, C-reactive protein=5 mg/L, calcemia=18 mg/dL, glosse exudate and culture on Sabouraud medium=negative, sterile urine culture, positive HBsAg, CD4=361 cells/µL, VL=672 copies/µL. Gynecological examination: pregnancy 8 weeks in evolution. Counseling was pregnant and gave very good compliance and
adherence to treatment. In February 2012 scheduled cesarean delivery: girl of 2800 g which until now (has 2 years) is clinically healthy, HIV negative. Father of daughter is in our records since 2000 with HIV-infection, under ARV therapy, combivir-nevirapine (CBV+NVP) with very good adherence to treatment, CD4=658 cells/µL, VL=undetectable from 2009 to the present. There were no reported side effects of ARV therapy administered (CBV+KAL) and immunological tests showed a clear improvement (CD4=420 cells/µL, VL=220 copies/mL). Combination ARV therapy (CBV+KAL) associated with good compliance and adherence to treatment in pregnant women ensures optimal control of immunity.

P47
Controversies in the management of HIV-positive adults and review of the literature - a case report
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Major HIV/AIDS organizations provide resistance testing guidelines, but the recommendation in chronically infected and treatment-naïve patients is controversial. We present a case including HIV resistance reports and review of the literature.

A 27 year old man was diagnosed with HIV 8 years ago, when nadir CD4 was 5/cumm. He experienced 3 antiretroviral combinations with reverse-transcriptase nucleosides inhibitors and protease inhibitors. Although he is adherent and his immunity was improved, undetectable HIV-RNA was never achieved. In January 2013 he presented with increasing viral load to 14,228 copies/mL and decreasing immunity more than 10%. The genotyping resistance testing assay was performed on HIV-RNA. A large number of genotyping mutations were found, significant for resistance to most nucleoside reverse transcriptase inhibitors and protease inhibitors. Although the patient has never been exposed to non-nucleoside reverse transcriptase inhibitors, the mutation K103 was also present. The review of patient’s history revealed HIV positive ex-wife who died in 2008. She had received antiretroviral therapy as part of one from seven antiretroviral experienced combinations. An identical pattern of genotyping resistance with the isolate of our patient, including the mutation K103, was revealed. His present wife is HIV negative and she is planning to become pregnant, but recommendation of pre-exposure prophylaxis is controversial. Large use of non-nucleoside inhibitors in Romania justify routine resistance testing of new HIV infected patients, especially if they are partners of antiretroviral experienced patients.

An obstacle to overcome: cerebral toxoplasmosis in patients living with HIV
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Toxoplasmosis represents the most frequent complication affecting the CNS of AIDS patients. In Europe and South America the prevalence of toxoplasmosis is higher than in the United States (50-75% to 15%), so the risk for the AIDS-associated toxoplasmosis is higher in this area, including Romania. Most of the AIDS patients have immunoglobulin G antibodies anti-Toxoplasma in their serum, like in the general population, so most of the cases represent a reactivation of a latent infection. We present a series of 5 cases with patients, aged between 19-29 years old, who developed cerebral toxoplasmosis. Three of the patients are multi-experienced, and for two patients the cerebral toxoplasmosis was the defining AIDS infection. Three patients had a CD4 count under 100 cells/cumm at the moment of their diagnosis, with low adherence for CART and for the prophylaxis with trimethoprim-sulfamethoxazole.

All patients but one had detectable HIV viral load. Two of the patients are positive for B hepatitis, one of them also for hepatitis D.

The clinical manifestations were persistent headache, confusion, lethargy, hemiparesis. All patients presented high levels for immunoglobulin G anti-Toxoplasma at the moment of the clinical manifestations, one patient presented immunoglobulin M anti-Toxoplasma.

The MRI examinations revealed characteristic multiple lesions. The treatment was performed using trimethoprim-sulfamethoxazole for 6 weeks. The evolution of the patients under the treatment was favorable for all the patients, with the remission of the symptoms and without neurological complications; they received trimethoprim-sulfamethoxazole prophylaxis until their CD4 >200/cumm, for another three months.

Although difficult to diagnose, cerebral toxoplasmosis is treatable and curable, despite of all the associated AIDS pathology.

P49
Generalized Molluscum contagiosum in an HIV infected patient
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Molluscum contagiosum is a benign contagious disease caused by a poxvirus. In an immunocompetent host molluscum contagiosum is most frequently a self-limiting benign viral disease of the skin and rarely of the mucous membranes. Atypical forms of molluscum contagiosum may be challenging to diagnose and are found in immunocompromised patients where they indicate severe impairment of cellular immunity. We report the case of a 45-years old patient admitted in our department in January 2014, for skin-colored and violaceous, painless papules and nodules on the arms, forearms, chest, face, inguinal and genital regions; the lesions appeared about 6 months ago, on the upper limbs and progressively extended. The patient was diagnosed with HIV infection in 2011, but did not follow antiretroviral therapy and never submitted to control until January 2014. In January 2014: CD4: 40 cells/µL, viral load: 112,617 copies/mL. He received antiviral therapy with acyclovir topical local therapy and antiretroviral treatment and evolution was favorable.

P50
Adult cell leukemia (ATL) in a patient with HTLV infection - case presentation
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Infections with human retroviruses, others than the HIV virus, are not very well known in Romania, despite the fact that screenings for HTLV I and II are constantly performed in blood donation centers. The authors draw attention on the possible severe consequences that may occur in chronic infections with these viruses by presenting the case of a 35-year-old male, who was known to be infected with HTLV I virus for several years and who consequently developed adult cell leukemia.

The authors also plead for the development of an algorithm for the detection, surveillance, monitoring and treatment of HTLV infections, throughout interdisciplinary cooperation between infectious disease specialists, hematologists, dermatologists. The authors strongly recommend the development of means to promote prevention by: securing blood transfusions; forbidding breastfeeding in women who tested positive for HTLV; using condoms in order to prevent sexual transmission in discordant couples.

Cite abstracts in this supplement using the relevant abstract number, e.g.: Colan et al. Adult cell leukemia (ATL) in a patient with HTLV infection - case presentation. BMC Infectious Diseases 2014, 14(Suppl 4): P50