early years of the epidemic when the leading risk factor was intravenous drug use, the population of HIV genetic variants was characterized by a high degree of homogeneity, with subtype was A1 being the most prevalent. In the late 90-es the recombinant form CRF03_AB was first registered in the Kaliningrad region; later on it was found as rare cases in all fUSSR countries, including Russia, and caused the outbreak in the city of Cherepovets in 2006. In addition, CRF02_AG recombinant, presumably originating from Cameroon, where this variant is quite widespread, was found in 2005 in Uzbekistan.

The purpose of this study was to conduct an analysis of prevalence and nature of HIV-1 recombinant forms in Russia and fUSSR countries at the present time.

Methods: From 2008 to 2015 years, 1347 sequences of HIV-1 *pol* gene from patients from Russia, Kazakhstan, Kyrgyzstan and Armenia were analyzed in the laboratory. The sequences were obtained using ViroSeq HIV-genotyping system, as well as *in house* method. Genotyping and phylogenetic analysis were performed using the COMET HIV-1 / 2v.0.5, MEGA 6.06 and PhyML program. There were 141 recombinant forms found among the samples analyzed. In addition, 50 pol gene sequences of HIV-1 recombinants from GenBank (Russia, Ukraine, Belarus) were included into this study.

Results: Three groups of circulating recombinant forms were found among the HIV-1 *pol* gene sequences analyzed — CRF02_AG (102/191, 53,4%), CRF03_AB (37/191, 19,4%) and CRF63_02A1 (42/191, 22%) — the double recombinant generated by viruses belonging to subtype A1 and CRF02_AG, as well as 10 unique recombinant forms of the same origin. All CRF02_AG sequence from Russia and FSU without exception clustered with the variant of Uzbekistan.

The frequency of recombinant forms of HIV-1 differed in different countries: we found 45,6% of them in Kyrgyzstan, 34,6% in Kazakhstan, 2,9% in Armenia and 4,5% in Russia.

Conclusion: Currently, the widespread of HIV-1 recombinant forms can be traced in all fUSSR countries and Russia, thereby increasing its diversity, with the appearance of unique recombinant forms. In general, it may be associated with the increased activity of migration, and with the active co-circulation of different HIV-1 genetic variants in the population.

Comparative analysis of AFSU HIV-1 variants circulating in IDUs and heterosexua populations

A.Lebedev, E.Kazennova, M.Bobkova
Moscow, Russia

Introduction: The large-scale epidemic of HIV-infection in Russia started when AFSU (IDU-A) subtype A1 HIV-1 variant was introduced into the population of injecting drug users (IDUs) in 90-s, and was characterized with the rapid distribution in this risk group together with the very low (1–2%) of the genetic differences between the viruses circulating in the population. Since the beginning of the 2000s the output of the virus outside the risk group specified was noted, with the gradual spread of AFSU variant through the heterosexual contacts whose share reached 37% among HIV-infected persons in 2015.

The aim of the present study was to compare the rate and nature of AFSU divergence over time in the main risk groups using the well-studied example of HIV-infection epidemic in the Perm region.

Materials and methods: Blood samples from 142 naive HIV-infected patients from Perm who were infected between 1996 and 2011 were collected, of which 91 belonged to the IDUs risk group and 51 were heterosexuals. The fragments of *pol* gene (PR-RT, 954 bp) and *env* (C2-V4, 498 bp) was obtained by the «nested» PCR, followed by sequencing. Phylodynamic analysis was carried out using Beast software package v 1.8.2 (http://beast. bio.ed.ac.uk). Reconstruction of the most recent common ancestor (tMRCA) and divergence estimation were performed using MEGA 6.0 program (http://megasoftware.net/). The search for the codons positive with regard to selection was carried out using DataMonkey (http://datamonkey.org); glycosylation sites were searched using the programs N-GlycoSite (http://hiv.lanl.gov) and NetPhos 2.0 (http://cbs.dtu.dk).

Results: The average genetic distance among all AFSU samples studied (142) and their tMRCA increased with time ($r=0,71$; $p<0,001$) and from 1996 to 2011 rose from 1,75 to 3,02% and from 2,98 to 6,29% in *pol* and *env* genes, respectively. The average rate (±SE) of the *pol* gene fragment evolution in A_{FSU} variants circulating in 2003–2011 among IDUs (n=57) and heterosexuals (n=51) was $1,83\pm0,13$ ($\times10^{-3}$) and $2,78\pm0,10$ ($\times10^{-3}$) substitutions per site per year, respectively. The similar index for the *env* gene fragment was $2,73\pm0,17$ ($\times10^{-3}$) and $6,18\pm0,14$ ($\times10^{-3}$) substitutions per site per year for IDUs and heterosexuals, respectively. Positive selection at the level of 6 codons was detected in the *pol* gene, with three differing positions depending on the risk group. There were 21 such codons detected within env gene, with the differences between the risk groups in 14 positions. The profile and frequency of 17 glycosylation sites in *env* gene showed no differences between the virus variants circulating in different risk groups.

Conclusions: Analysis of the genome of A_{FSU} HIV-1 viruses circulating in the region shows the unequal rate and nature of the diversity both in different viral genes and between different risk groups.

The *pol* and *env* genes evolution demonstrates the presence of a temporary structure with a characteristic increase of divergence between viruses and their last common ancestor, which grew by 1,7 (for the *pol* gene, p<0,001) and 2,4 times (for the *env* gene, p<0,001) during the observation period. The unequal rate of spread of HIV in these high-risk groups, and as a result, differences in the degree of selective pressure of the immune system onto the virus population, possibly causes two effects. On the one hand, it may cause a higher rate of evolution of viruses that spread among the heterosexuals, which is 1,5 times higher than in IDUs for *pol* gene (p<0,001) and 2,1 times for the *env* gene (p<0,001), on the other hand — the differences in positive selection effect on the individual sites, with the frequency of amino acids in these positions among different risk groups being the same (as a whole).

Malignant neoplasms in HIV patients

A.V.Nekrasova, V.V.Rassokhin, Ye.V.Stepanova, O.N.Leonova, S.A.Buzunova
St.-Petersburg, Russia

Background: HIV patients are at high cancer risk; therefore, oncological care provision to them is becoming a priority. Objective: To study the clinicoepidemiologic characteristics of cancer in HIV patients, to assess their total survival rate (TSR), and to determine what factors influence TSR and interfere with anticancer therapy.

Patients and methods: The study involved 192 HIV patients with cancer who were treated at Saint-Petersburg AIDS Center in 2006–2014. Their case histories were examined in conjunction with Population Cancer Register data. The median follow-up time of the survived patients (n=73) was 2 years and 8 months (range: 1 month to 13 years). In 36% of the patients, their follow up period was more than 5 years. Results: The median age of male patients (n=142) was 34 years (range: 17–78 years). HIV was detected before cancer in 93%, and concomitantly with cancer, in 7% of the cases The median duration of HIV infection before cancer diagnosis was 5 years (range: 3 months to 19 years). Cancer was found at stages 4b or 5 according to (Pokrovsky, 2001) in 95% of cases. At the time of cancer diagnosis, ART was administered in 9,4% of cases, viral load was suppressed (HIV RNA <50 mL^{-1}) in 7,8%, and the median CD4 cell count was 100 μL^{-1} (1–1184). The most prevalent among cancers were lymphomas (n=111, 58%). At the time of diagnosis, Stage 4 cancer (TNM, Ann Arbor) was found in 80%, complications in 15,1%, and more than three complications, in 6,8% of cases. In total, 57,3% of the patients had conditions that limited anticancer therapy: CD4-cell counts below 50 μL^{-1} (28,6%), severe opportunistic infections involving CNS (28,5%) and lungs (23%), active tuberculosis (12%), WBC below 1000 μL^{-1} (3%), and Stage 4 thrombocytopenia (platelet counts below 20 000 μL^{-1}; 2,6%). Opiate-addicted patients in the non-abstinence state or alcoholic patients made 14%. TSR in HIV patients was 55% during 1 years and 39% during 5 years after cancer diagnosis. The factors that reduce TSR during 5 years include severe opportunistic infections involving the CNS (20% vs 47%, p<0,001) and the lungs (17% vs 46%, p<0,001), the long duration of HIV infection before cancer diagnosis, CD4-cell count (less than 50 vs 250 mL^{-1}), HIV RNA (above 400 vs. below 50 copies per 1 μL). Being coinfected with EBV, CMV, HCV, or HBV did not influence TSR during 5 years. ART prescribed upon cancer diagnosis improved TSR during 5 years (49% vs 20%, p<0,001), fig. 2. Conclusions: Lymphomas are the most prevalent cancer in HIV patients (58%). Most cancer are diagnosed at advanced stages (80%). In 93% of cases, HIV infection is diagnosed before cancer, ART being provided to only 9,4 of the patients. Conditions that limit anticancer therapy were found in 57,3% of HIV cases. The total 5-year survival rate in HIV patients after cancer diagnosis is 39%. ART prescribed upon cancer diagnosis significantly increases this parameter.

Structural brain changes in the early stages of HIV

E.P.Magonov, T.N.Trofimova
St.-Petersburg, Russia

Motivation: HIV causes neurological complications with the title «HIV-associated neurocognitive disorder (HAND)». HAND occur in 50% of patients which presents a strong social problem. After the introduction of HAART (1996) the number of cases of HIV-associated dementia significally reduced, but the total number of neurocognitive disorders was not decreased.

Study aim: improve early diagnosis and monitoring of atrophic brain changes in HIV patients using quantitative evaluation methods of MRI images.

Study tasks: Further investigate changes in global and regional brain structures in HIV-infected patients in the early stages of the disease; to study the relationship between atrophic and functional changes of brain structures in HIV-infected patients in the early stages of the disease.

Patients: 24 to 48 y.o in early stage of HIV without opportunistic infections and brain lesions according to conventional MRI, no drug addicts, no hepatitis, no psychological disorders. CD4 level: 445±230 cells/ml. Disease duration: 6 to 18 months.

MBaRsIe apcrqotuoicsoitli on protocol:

Pulse sequences	Time (minutes)
Localizers	1:37
Ax T2	1:48
Sag T2	2:12