below 5% with effective interventions. Placenta plays an important role in the prevention of the mother-to-child transmission (MTCT) of HIV during pregnancy. The immune parameters of the placenta of the HIV-infected woman during pregnancy have been linked to the mother-to-child transmission of HIV. The purpose of this study was to investigate the characteristics of the placentas and the expression of the CD14+ and CD68+ receptors in macrophages of the placenta of Russian HIV-infected women and to compare it with the expression of the immune receptors in placentas of women with co-infections and healthy women as controls.

*Methods:* The study prospectively investigated postpartum placentas obtained from deliveries at two different (general and specializing in HIV-complicated deliveries women) maternity wards in St.-Petersburg. Data on maternal age and delivery outcome were collected. The placentas were collected from three groups of patients: Group A — cases with children infected with HIV, Group B — cases with non-infected children born to HIV-infected mother and Group C — placentas from women without any infection.

In morphological analysis routine staining (hematoxylin and eosin) and microscope investigation were used. HIV-infection was confirmed immunohistochemically with use of p24 antibodies (Dako). The DNA-viruses of family *Herpesviridae* was detected immunohistochemically with use of antibodies against HSV (I and II) and CMV (Diagnostic BioSystems). Receptors expression was studied immunohistochemically with use of monoclonal antibodies CD14 (Novocastra) and CD68 (KP1 clone, Dako) and further morphometric analyses with the program Leica QWin Standard v2.8. Results: The study collected 11 placentas in Group A, 11 placentas in Group B and Group C had 16 placentas. The mean birth weight in Group A was 2965 ($\pm$SD=661) gm, in Group B 3056 ($\pm$560) gm and in Group C (3536$\pm$306 gm). The average weight of placentas was lower in Groups A and B (434$\pm$48 gm and 445$\pm$55 gm, respectively) compared to Group C (566$\pm$59 gm).

Placental infection was detected in 91% (n=10) of placentas Group A, 64% (n=7) of Group B. In Group A the majority of placental inflammation (73%; n=8) represented inflammatory changes (chorioamnionitis, placental membrane inflammation), including 46% (n=5) combined bacterial and viral changes, and 18% (n=2) had isolated viral inflammatory changes — HIV and DNA-virus (one with HSV-1, two with CMV, and one with combined HSV-1 + CMV). In Group B the majority of placentas had HIV changes — 55% (n=6) and the smaller proportion — 18% (n=2) had combination of viral and bacterial infection associated changes. The presence of the bacterial and viral inflammatory changes was statistically associated with MTCT ($p<0,05$). The chronic insufficiency of placenta was detected in Group A in 45,5%, in Group B in 36% (n=4). HIV RNA effects were detected in villous chorion of all placentas in Group A and Group B with positive p24 antigen. Expression of CD14+ in cytoplasm of chorion villi cells and endotheliocytes was the highest in Group A (14,14$\pm$1,11%), followed by Group B (10,04$\pm$1,37%), when compared with control Group C (3,21$\pm$0,43%, $p<0,05$ for both comparisons). Similarly, the expression of CD68+ was the highest in Group A (13,07$\pm$0,83%), followed by Group B (7,21$\pm$0,89%) when compared to the control Group C (2,02$\pm$0,60%, $p<0,05$ for both comparisons).

*Conclusion:* In our study there was a significant prevalence of bacterial and combined bacterial and viral inflammatory changes in the placentas of women with MTCT of HIV compared to the placentas of the women without MTCT. Further studies of the role of the placenta may help to better understand the mechanisms of the vertical transmission of the HIV. The presence of viral infections (HSV and CMV) and HIV was accompanied by the significant increase of CD14+ and CD68+ macrophages in the placenta of Russian women at time of delivery. Further studies of the role of the immune factors of the placenta may help to better understand the mechanisms of the transmission of the HIV viruses to the infants of the infected women.

## The epidemic of comorbid and advanced stages of HIV infection in the Northwest of Russia

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*Background:* The numbers of registered HIV cases and advanced forms of HIV infection and the rate of deaths caused by the infection are increasing in Russia. In 2015, high HIV prevalence (more than 0,5% of the total population) was reported in 26 regions of Russia where 41,5% of population reside. The aggravation of epidemic situation is associated with not only increasing HIV prevalence and HIV-caused death rate but also with increasing HIV expansion from high-risk groups to the general population.

*Objective:* To assess the dynamics of the development of HIV epidemic, including the comorbid forms of HIV infection, in the Northwest of Russia from the time of detecting the first HIV cases up to the present, in particular in the recent years.

*Tasks:* To study HIV epidemic in the Northwest Federal Region; to determine the main causes of the increasing HIV incidence, the development of comorbid forms of HIV infection, and the increasing HIV-associated mortality; and to pinpoint the specific features of diagnostics, course and severity of HIV infection at different times before the onset and in the course of antiretroviral therapy.

*Materials and methods:* Reviewing of outpatient clinic records, case histories, and AIDS Center reports in the Northwest of Russia in association with studies of the clinical conditions of HIV patients encompassed 120 000 HIV cases. The data were treated statistically using MS Excel and Statistica 10 and software tools.

*Results:* The onset of HIV epidemic dates back to late 1990s when new found HIV cases amounted to hundreds and, further on, to thousands because of rapid spread of injection drug use with HIV-contaminated needles and syringes. At the time of diagnosis, most patients had normal CD4 cell counts suggesting a recent HIV infection, which had reached Stage II or III.

In 2003–2004, the epidemic subsided, having involved mostly men aged 20 to 25 years, who constituted the main group of HIV risk and at difference from the earlier time were infected with subtype A HIV-1 (more than 90%). The decline of the first wave of HIV incidence may be explained by the exhaustion of the main risk group and by the active preventive interventions. In the Northwest of Russia, the most vulnerable to HIV were territories featuring higher population density and more intense migrant streams (Saint-Petersburg and Leningrad, Kaliningrad, and Murmansk Oblasts).

In patients who according to the presence of opportunistic and concomitant diseases could be referred to HIV infection Stages 4 or 5, blood CD4 cell counts were below 200 $m1^{-1}$, and HIV loads were $10^{4,5}$ to $10^{6,0}$ RNA copies per 1 ml. The duration of infection from the time of HIV contracting, mainly by the injection route, to HIV detection was from 4 to 12 years, probably because a part of HIV cases detected during the first peak of the epidemic were not diagnosed timely. Other patients were infected in a relatively more recent time, during the second wave of HIV. The least numerous group comprised patients at advanced stages associated with immunosuppression who needed HAART at the time of diagnosis. The high numbers of HIV cases at Stage 4 was conducive to tuberculosis and associated with high death rate over the first year after the onset of therapy.

Lethal cases were registered in patients under HAART mainly because of pronounced immunosuppression, the development of severe concomitant infections including tuberculosis, patients' poor adherence to therapeutic regiments, and the discontinuation of therapy.

*Conclusion:* The current period of HIV epidemic may be characterized as associated with the advances stages of HIV infection associated with numerous concomitant diseases and high death rates upon HAART. All this warrants special attention to early HIV detection and subsequent management of HIV cases and to developing of a complex of preventive, organizational and socio-medical interventions adapted to megalopolises as well as to sparsely populated territories.

**Novel dual inhibitors targeting HIV-1 integrase and reverse transcriptase-associated ribonuclease H activity**

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Reverse transcriptase (RT) and integrase (IN) facilitate the early stages of HIV-1 replication. HIV-1 integrase (IN) and reverse transcriptase (RT)-associated ribonuclease H (RNase H) domains belong to the polynucleotidyl transferase superfamily and share common structural features. The catalytic sites of both enzymes contain a central core composed of three highly conserved amino acid residues forming the DDE motif or RNase H-like fold (Asp, Asp and Glu). Among the novel approaches aimed to identify new HIV-1 inhibitors, the development of dual-action inhibitors, single drugs that may act on two different enzymes, such as IN and RNase H. A number of attempts has been made to identify compounds that may act on both enzymes, but still there is no dual inhibitor passed the clinical trials [Corona A., et al. *Antomicrob. Agents Chemother.*, 2014, 58 (10), 6101–6110; Cuzzucolli Crucitti G., et al. *J. Med. Chem.*, 2015, 58 (4), 1915–1928; Esposito F., et al. *Antiviral Chem. Chemother.*, 2014, 23, 129–144].

In our previous works, we have studied in detail the integration inhibition by dimeric bis-benzimidazoles (DBI) [Zhuse A.L., et al. *J.Biomol. Struct. Dyn.*, 2007, 24(6), 666–668; Korolev S.P., et al. *Russian J. of Mol. Biol.*, 44 (4), 633–641.]. The inhibitory effect of these compounds are explainable by the fact that they interfere with a correct binding of the DNA substrate in the IN active center. To enable their potential use however requires to overcome their low solubility in water and to increase their bioavailability. Recently the new series of water soluble DBI has been obtained. The inhibitory activity of these compounds was determined for both recombinant enzymes IN and RNase H. It was shown that the inhibition ability for the set of compounds depends on the length of the spacer connecting the pairs of benzimidazole fragments. The $IC_{50}$ values of the most active one were 50 nM for IN and 5 μM for RNase H. Moreover these compounds demonstrated extremely low cytotoxity ($CC_{50}$>100 μM). According to preliminary trials the most active DBI showed its inhibitor activity on replication-incompetent VSV-G-pseudotyped vector HIV-1 based. Overall, DBI may be considered as a potent dual-acting inhibitor for treatment of HIV-1 infections.

**Inorganic pyrophosphate analogs as multitarget HIV replication inhibitors**

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Despite the undoubted success in the development of human immunodeficiency virus type 1 (HIV-1) therapy, this