7. HIV, HEPATITIS AND OTHER SOCIALLY SIGNIFICANT INFECTIONS

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THE ANALYSIS OF TRANSMITTED HIV-1 VARIANTS AMONG ACUTELY INFECTED PEOPLE WHO INJECT DRUGS USING NGS APPROACH

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The phenomenon of a genetic bottleneck, i.e. transmission of one or a few variants of the virus, has been widely studied for sexual transmission, but for people who inject drugs (PWID) the available data are not concludive.

The objectives of the study were real-time detection and follow-up of individual cases of acute HIV-1 infection (AHI) and analysis of the genetic variability with SGA and NGA approaches.

We analyzed full-length *env* genes of transmitted strains using single genome amplification (SGA) and Bayesian Evolutionary Analysis Sampling Trees (BEAST) approach. We also implemented the PrimerID Illumina MiSeq approach for ultra-deep sampling of a fragment of the *env* gene to look for the presence of minor transmitted variants.

Among PWID screened for the study 25% were seropositive. The calculated AHI incidence was 9.3 per 100 person-years. We report 7 cases of acute HIV-1 infection among active PWIDs and 8 potential sexual partners of PWID. Among all the cases studied by SGA and Primer ID approaches we detected a homogeneous viral population likely produced from a single viral variant.

We also detected one case of a secondary infection from a different donor. Adding to previously published data we have analyzed 19 cases of AHI subtype A in St. Petersburg, and at least 74% had a homogeneous viral population confirming a strong genetic bottleneck during parenteral transmission.

The data confirm our original discovery of the genetic bottleneck in HIV transmission among PWID.

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VIRAL HEPATITIS B AND C IN THE ARKHANGELSK REGION: LONG-TERM DYNAMICS OF INCIDENCE AND CROSS-SECTIONAL STUDY OF MARKERS AMONG ADULT POPULATION

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Viral hepatitis B and C (VHB and VHC) represent a serious problem for national health care, affecting the young working population of the country.

The purpose and objectives were to analyze the long-term incidence of VHB and VHC in the Arkhangelsk region and to study the prevalence of VHB and VHC markers among adult population in Arkhangelsk city.

The statistical data forms reported to the federal level were used and a population-based study was carried out as a part of the Norwegian-Russian project. A quota sampling method was used to recruit 1243 adults aged 18–39 years. All participants were tested on VHB Antigen (HBsAg), VHB core antibodies (anti-HBc), VHB surface antibodies (anti-HBs) and VHC (sum antibodies) using an enzyme-linked immunosorbent assay.

Over the past 30 years, the incidence of acute VHB (AVHB) in the Arkhangelsk region decreased in 40 times, the incidence of chronic VHB (CVHB) — in 2.8 times. Nowadays, the incidence of CVHB is in 15 times higher compared with the incidence of AVHB; the incidence of CVHC is in 87 times higher compared with the incidence of AVHC. The prevalence of VHB markers (HBsAg and/or anti-HBc) was 11.8% in men and 10.2% in women in a population-based study. Among men, 1.1 and 1.3% of women were positive on HBsAg; 41.8% of men and 50.9% of women were positive only on anti-HBs. All three tests were negative in 46.4% of men and 38.9% of women. Among men, the percentage of positive for VHC markers was 6.4%, among women — 4.3%. Co-infection of VHB and HCV was found in 1.5% of men and 0.3% women.

Despite the progress made in the control of VHB and VHC, a pool of sources of infections remains in the population. Therefore, preventive work should be continued.

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IMMUNOPATHOGENESIS HIV AND MATHEMATICAL MODELING

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The study of HIV immunopathogenesis is the most important prerequisite for the search of new and improving the existing antiviral and immunomodulating medicines and vaccines used for the treatment and prevention of HIV infection.

The accumulated data of the HIV infection and the functional human physiological system reactions on it indicate that multifactorial mechanisms, which determine the development, course and outcomes of HIV infection, are mediated by a great number of physiological and pathological processes with various positive and negative feedbacks.

Due to the complexity of HIV interactions with the human body, the completely new interdisciplinary and interdisciplinary approaches are in urgent need. These approaches should include various bioinformatics and system analysis methods for the identification of immunobiological protection factors in HIV infection and comprehensive understanding of its pathogenesis. Thus, the advances in genome screening for the cellular proteins with anti-HIV activity identification may serve as the base for the promising approach for the HIV treatment and prevention. In turn, the methods of multiscale mathematical modeling

should be used to solve the tasks of characterization and conceptual analysis of meta-data on the "HIV-host" interaction system. The multiscale mathematical modeling methods may help in the studies focused on the sensitivity of viral infection "stabilization points" towards virus replication and immune reactions in the acute phases of infection. Moreover, the these methods are necessary for the estimation of prolonged ongoing immune stimulation effects, the degree of damage to microenvironment and tissue structures of lymph nodes, and the decrease in proliferative potential and the pool of central $CD4^+$ T-cells.

Lastly, the special emphasis isgiven to the theoretical analysis of HIV relationships with macroorganism, taking into account the virus evolution in the conditions of lymphocytes and macrophages phenotype changes during the adaptive reconstruction of the immune system.

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CHALLENGES AND PERSPECTIVES IN HEPATITIS C VIRUS (HCV) RESEARCH IN AN ERA OF DIRECT ACTING ANTIVIRAL (DAA) THERAPY

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Elaboration of *in vitro* models enabled studies of the HCV life cycle and a search of inhibitors of viral replication, leading to the development of effective DAA targeting non-structural proteins involved in virus replication (NS3/NS4A protease, NS5B polymerase and NS5 inhibitors) with cure rates of more than 95%. Despite this outstanding success of modern medicine and substantial progress in our knowledge of the virus, infection control might be only effective when antiviral therapy and vaccination are combined, since individuals that have been cured with DAAs remain susceptible to reinfection. Another limitation of DAA is their low genetic barrier, resulting in the emergence of drug escape-variants. Alternative or complementary approaches have been thus considered to target host factors required for accomplishment the virus life cycle: cell entry, assembly or release, related to lipoprotein metabolic pathways. Such drugs would have high genetic barrier and pan-genotypic activity.

HCV represents a difficult target for vaccination due to its considerable variability (7 genotypes, 67 subtypes and genetically diverse "quasispecies"). Continuous mutations result in changes in E1E2 envelope glycoproteins targeted by neutralising antibodies and help HCV to evade humoral immunity. The structure of HCV particles circulating in the blood of infected patients remains elusive due to their association with very low-density lipoproteins (lipo-viro-particles). Moreover their size and composition evolve during infection. Shielding of the envelope epitopes by lipoproteins and glycoproteins, cell-to-cell virus spread, and its dissemination by exosomes represent important escape mechanisms that contribute to propensity of HCV to establish chronic infection.

The development of HCV vaccine requires better understanding how antibodies interfere with the virus and of the mechanisms of CD4 T helper cell failure during infection, a predictor of progression to chronicity. An HCV vaccine eliciting T cell responses rather than neutralising antibodies is considered and is currently in clinical testing. Notably, the goal of vaccination is a partially protective vaccine, able to prevent development of persistence, not necessarily infection. A vaccine might be equally needed to restore immune dysfunction of cured patients to prevent re-infection. The development of permissive and immunocompetent animal model(s) is required for further studies of HCV vaccines and HCV-related pathogenesis.

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FREQUENCY AND THE CLINICAL SIGNIFICANCE OF OCCULT HEPATITIS B VIRUS INFECTION

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The detection of hepatitis B virus surface antigen (HBsAg) in serum remains the mainstay in the diagnosis of chronic hepatitis B viral infection and screening for hepatitis B virus in most developing countries, include Russia. Symptoms in chronic hepatitis B viral infection may range from mild nonspecific symptoms in patients with minimal liver damage to ascites, peripheral edema, and encephalopathy in patients with advanced liver disease. Anti-HBc may be the sole marker of resolved hepatitis B viral infection, as anti-HBs, which is neutralizing and so appears after the clearance of HBsAg, may disappear from serum many years after the resolution of hepatitis B viral infection. Occult hepatitis B viral infection is characterized by the absence of detectable HBsAg and present of HBcAb. The objective of study was to identify cases of occult hepatitis B viral infection from patients diagnosed with chronic viral hepatitis and determine it clinical significance.

2236 adult patients with chronic B virus infection were enrolled in study. Serological markers for hepatitis B virus were determined with immunoenzymatic assay and viral DNA — by polymerase chain reaction. For assessment of liver fibrosis was used transient elastography.

Out of all, 42.2% patients had tested negative for the HBsAg and positive HBcAb serologic marker. HBsAb (more 10IU/l) were detected in 28.1% occult hepatitis B. DNA of virus in blood was detected by polymerase chain reaction (threshold 100 IU/l) in 4.3%. In case of using the sensitive test system (threshold 10 IU/l) DNA was detected in 100%. ALT levels were different: N — in 21.8% patients, 1–2N — 41.7%, 2–5N — 27.0%, more 5N — 9.5%. The severe staging of liver fibrosis (F3-F4) is established in 55.5% (F3 — in 3, 6%, F4 — in 51.8%). The moderate staging of liver fibrosis (F1-F2) was 44.5% (F1 — 15.5%, F2 — 29.1%). The severity of chronic liver disease in terms of Child–Pugh score was: class A — 6.3%, class B — 15.5%, class C — 78.2% ($p < 0.001$). Mortality in the cohort of patients with occult hepatitis B virus infection was 13.2% and among patients with cirrhosis — 25.5%. Hepatocellular carcinoma was diagnosed among patients with liver cirrhosis in 1.8%.

The long-term persistence of the virus in the liver may induce a very mild but continuing necroinflammation that — if other causes of liver injury co-exist — may favor the progression of the chronic liver disease toward cirrhosis.

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HEPATITIS A PREVALENCE AMONG CHILDREN IN BOKE AND KINDIA PROVINCES (REPUBLIC OF GUINEA)

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There are no reliable statistical data on the hepatitis A reported cases number among the Republic of Guinea population, included children. One of the morbidity estimation method is the antibodies to hepatitis A virus prevalence estimation in different age groups. Aim of study: to estimate