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.

7.6 doi: 10.15789/2220-7619-2018-4-7.6

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

the seroprevalence of hepatitis A antibodies among children in Guinea by analyzing the detection of antibodies to hepatitis A virus in the local population. Materials and methods. The study was carried out in 2017 year in the Russian-Guinea Research Center for Epidemiology and Prevention of Infectious Diseases of Rospotrebnadzor (Kindia, Republic of Guinea) laboratory by St. Petersburg Pasteur Institute researches (St. Petersburg, Russia) with the assistance of the Republic of Guinea specialists. Serum samples were obtained from 71 conditionally healthy children living in the provinces of Boke (39 samples) and Kindia (32 samples) at the age 0–18 years (mean — 7.4±5.1 year), both sexes (male — 46.5%, female — 53.5%). There are no data about hepatitis A vaccination or case of hepatitis A in the past. Antibodies of the IgG class to hepatitis a virus were determined by enzyme immunoassay with the use of the test systems Vektohep A-IgG (manufactured by Vector-Best, Russia).

Antibodies of the IgG class to the hepatitis a virus were detected in 84.5% of samples. Seropositive persons at the age 0–5 years was 72.9% (95% CI: 55.9–86.2%), at the age 0–10 years — 77.6% (95% CI: 63.38–88.23%), at the 0–15 year — 83.0% (95% CI: 71.73–91.24%). The study was conducted in 1987–1988 years by A.P. Ivanov et al. showed the presence of antibodies IgG class to hepatitis a virus in children 0–10 years in 82.0% of cases, 0–15 years in 74.0%. There is no gender difference in antibody identification at the children 0–15 years (males and females 82.1% and 85.7% respectively, p = 0.5110), and among children 0–10 years (male and female — 76.2% and 84.0% respectively, p = 0.2167). In accordance with the WHO criteria, if antibodies detected in more than 50% of cases among children 0–15 years and less than 90% among children 0–10 years, this indicates the medium seroprevalence of hepatitis A in the population.

The prevalence of hepatitis A in accordance with our data, is at the middle level and has not significantly changed over the last 30 years.

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HIGH BURDEN OF HEPATITIS B IN VIETNAM: IMPACT OF A HIGHLY HETEROGENEOUS VIRAL POPULATION

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South-East Asia is highly endemic area for hepatitis B. In Viet Nam, 8.4 million individuals were estimated to live with HBV infection that resulted in 23 300 deaths in 2005. Here, we investigated naturally occurring genetic variants of hepatitis B virus circulating in general population in Viet Nam.

A total of 3080 adults of 18–79 years old from 16 regions (An Giang, Binh Duong, Dong Nai, Ha Giang, Hoa Binh, Hue, Kien Giang, Lam Dong, Kontum, Nghe An, Ninh Binh, Quang Tri, Thai Nguyen, Hi Phon, Kanh Hoa and Thanh Hoa) were enrolled in this study in 2012–2014. All serum samples were analyzed for the presence of HBsAg with Monolisa® HBsAg detection kit (Bio-Rad, USA) or rapid test (Alere Determine™ HBsAg, USA). As a result, 309 (10.03%, 95% CI, 8.99–11.15) out of 3080 adults were positive for HBsAg. HBV DNA was extracted from HBsAg positive serum samples. HBV genotypes were determined by phylogenetic analysis based on S or P genes.

A total of 117 HBV isolates were genotyped. Six HBV subgenotypes (B2, B4, B6, C1, C5; I) and two recombinant forms (B/C; C/B) were identified. Subgenotype B2 was found in 4 (3.42%, 95% CI 1.34–8.46) isolates; B4 — in 82 (70.09%, 95% C I 61.26–77.64); B6 — in 2 (1.71%, 95% CI 0.47–6.02); C1 — in 20 (17.09%, 95% CI 11.35–24.93); C5 — in 1 (0.85%, 95% CI 0.15–4.68); I — in 3 (2.56%, 95% CI 0.88–7.27); recombinant forms B/C — in 3 (2.56%, 95% CI 0.88–7.27) and C/B — in 2 (1.71%, 95% CI 0.47–6.02). The phylogenetic analysis revealed that Vietnamese HBV strains of subgenotypes B4, B2 and C1 formed the several distinct clusters that separated from other strains isolated in Asia. HBV strains belonged to other subgenotypes were scattered among Asian variants. Subgenotype I was found only in the northern mountain region. Based on "a" determinant in S protein the HBV strains were classified into four subtypes: adr, adw2, ayw1, ayw3. No amino acid substitutions, which may alter HBsAg antigenicity or be responsible for vaccine escape were detected in preS region as well as in major hydrophilic region of the S region.

The predominance of HBV subgenotype B4 in all studied regions indicates crucial impact of this HBV variant on the persistence infection in Viet Nam. The high genetic diversity of viral population highlights the multiple sources of infection, successful spreading of a variety of viral variants and provides insight into the driving force of the HBV epidemic process in Viet Nam.

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MOLECULAR-GENETIC CHARACTERISTICS OF THE HEPATITIS B IN THE NANAYSKY DISTRICT OF THE KHABAROVSK TERRITORY

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Hepatitis B continues to stay a pressing issue due to frequent development of chronic cases of the disease.

Aim of the research was to analyze the genetic diversity of the hepatitis B virus (HBV) circulating among the indigenous population of the Nanaysky District of the Khabarovsk Territory.

A total number of 82 samples (59 women, 23 men) of blood plasma were obtained from the Nanaysky District patients with the diagnosis of chronic hepatitis B (CHB). According to the ethnic composition, there were 62.3% of Nanai people, 32.9% of Russians, Udege and Evenks totaled by 2.4% each. The HBV DNA was detected using the PCR kits "AmpliSens®HBV-FL" and "AmpliSens®Monitor-FL" (Central research institute of epidemiology of the Rospotrebnadzor, Russia). The PCR was followed by genotyping using a two-step PCR with primers to a conservative region of overlapping S and P genes. Phylogenetic analysis was performed with the MEGA6.0 software. Neighbor-Joining method was used to build the phylogenetic trees. Nucleotide distance was estimated via Kimura method.

HBV DNA was found in 46 (56.1%) samples of the blood serum. The viral load levels in 13 (28.3%) patients was low (< 10^3 ME/ml), in 26 patients it was intermediate (10^3–10^6 ME/ml) and in 7 cases it was high (> 10^6 ME/ml). The phylogenetic analysis was performed for 43 nucleotide sequences. Genotype D was dominant and was found in 34