The 11-th Annual Conference of the Network against Life-threatening viral infections
Vilnius, April 24-27, 2014
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<td>Bartosch</td>
<td>Lyon</td>
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<td>Centre de Recherche en Cancerologie de Lyon/CRCL</td>
<td>HCV INFECTION REPROGRAMS THE HEPATIC GLUCOSE AND GLUTAMINE METABOLISM</td>
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<td>Francesco</td>
<td>Negro</td>
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<td>Switzerland</td>
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<td>IMPROVING VACCINE IMMUNOGENICITY AND DEVELOPMENT OF NEW ANIMAL MODELS OF HCV INFECTION</td>
<td><a href="mailto:lars.frelin@ki.se">lars.frelin@ki.se</a></td>
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<td>Britta</td>
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<td>VACCINE DEVELOPMENTS FOR VIRAL HEPATITIS AND HIV</td>
<td><a href="mailto:britta.wahren@ki.se">britta.wahren@ki.se</a></td>
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<td>Atlanta</td>
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<td>HEPATITIS B AND C - A SILENT EPIDEMIC</td>
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<td><a href="mailto:joakim.esbjornsson@imm.ox.ac.uk">joakim.esbjornsson@imm.ox.ac.uk</a></td>
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ABSTRACTS (alphabetic order) (P – poster)

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<td>Remy Andre Jean</td>
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<td>HEPATITIS MOBILE TEAM : A NEW CONCEPT FOR BENEFIT TOWARD DRUGS USERS WITH HEPATITIS C AND OUTSIDE SOCIAL AND MEDICAL TEAMS</td>
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<td>INFLUENZA, PANDEMRIX VACCINATION AND NARCOLEPSY – A REVIEW OF SOME RECENTLY PUBLISHED LABORATORY FINDINGS</td>
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HCV infection reprograms the hepatic glucose and glutamine metabolism

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Categories
hepatitis

Keywords
hepatitis C virus, metabolism, pathology, hepatocarcinogenesis

Abstract (english) (2099 characters)

Background and aims: Hepatitis C virus (HCV) is the only virus that is known to perturb hepatic glucose and lipid metabolism with important pathophysiological consequences. Chronic carriers often develop steatosis, insulin resistance and type 2 diabetes, which resolve with successful antiviral treatment. Therefore it is thought that HCV interferes directly with the lipogenic and glycolytic pathways and requires these changes for its replication. However, the exact circumstances of this metabolic reprogramming still remain vague and require further analysis. Here we investigate some fundamental changes in glucose and glutamine metabolism linked to HCV infection.

Methods: RNA derived from Huh7.5 cells infected or not with JFH1 and from biopsies of chronic HCV patients were used for RT-qPCR analysis with primers targeting metabolic genes. Nutrient deprivation and biochemical and NMR-based metabolic flux analysis were performed with JFH1 infected Huh7.5 cell culture extracts.

Results: We show that HCV modulates the transcript levels of some key regulators of glucose metabolism in the hepatocyte-derived cell-line Huh7.5 as well as liver biopsies of patients with chronic hepatitis C, which hints at changes to glycolytic fluxes. In addition, we found enzymes and factors regulating the glutamine metabolism (MYC, SLC1A5, SLC7A5, GLS) to be induced by HCV in vitro and in liver biopsies of chronic HCV carriers. This correlated with altered metabolite fluxes in HCV infected cells, which were quantified by NMR flux analysis. Furthermore, cell proliferation rates of HCV infected and uninfected cells in conditioned growth media showed that infected cells become dependent on glutamine and reduce their glucose dependence. We show furthermore that silencing of glutaminolytic genes as well as of MYC, an oncogene and metabolic transcription factor known to induce glutamine addiction, reduced HCV infection.

Conclusions: Altogether, these data suggest that HCV reprograms the hepatocyte metabolism and establishes glutamine dependence. This HCV-induced metabolic reprogramming is similar to that commonly found in many types of tumor cells. Because these changes seem to be required for viral replication, we are currently investigating their roles in the various steps of the viral life cycle, and their impact on the pathological features associated with chronic hepatitis C.
Impact of different risk factors of fibrosis progression in chronic hepatitis C

Abstract (english) (1857 characters)

The natural course of hepatitis C varies widely. To improve the profiling of patients at risk of advanced liver disease, we assessed the relative contribution of factors for liver fibrosis progression in hepatitis C. In a cross-sectional study of the Swiss Hepatitis C Cohort, we analysed 1493 chronic hepatitis C patients with an estimated date of infection and at least one liver biopsy. Risk factors for accelerated fibrosis progression rate (FPR) (≥0.13 Metavir fibrosis units per year) were identified by logistic regression. Factors included age at infection, sex, HCV genotype, BMI, significant alcohol drinking (≥20 g/day for ≥5 yrs), HIV coinfection and diabetes. In a subgroup of 590 patients, we assessed the impact of SNPs previously associated with fibrosis progression in GWA studies. Results were expressed as attributable fraction (AF) of risk for accelerated FPR. Age at infection (AF 28.7%), sex (AF 10.8%), HCV genotype (AF 9.4%) and significant alcohol consumption (AF 2.4%) contributed to accelerated FPR, while anti-HIV, diabetes and BMI did not. In the 590 genotyped patients, variants at rs9380516 (TULP1), rs738409 (PNPLA3), rs4374383 (MERTK) (AF 19.2%) and rs910049 (MHC region) significantly added to the risk of accelerated FPR. Results were replicated in three independent cohorts from France, the US and Australia totalling an additional 1084 patients, and a meta-analysis confirmed the role of age at infection, sex, HCV genotype, rs738409, rs4374383 and rs910049 in accelerating FPR. The role of excess alcohol consumption was confirmed only when host genetic factors were not considered. In conclusion, our study shows that most factors accelerating liver fibrosis...
progression in chronic hepatitis C are unmodifiable. These results have obvious and important consequences on the management of chronic hepatitis C patients.
EDCTP as a model of Europe-Africa partnership for HIV/AIDS research – achievements and future directions

Invited Abstract
No 3

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Categories:
SOCIAL ASPECTS OF MEDICAL RESEARCH

Presentation type: Oral

Contact: Breugelmans@edctp.org

Submission date: March 2014

Abstract (english) (2099 characters)

Problem statement
HIV infection remains a major public health concern and poses challenges that go beyond the capacity of individual countries. More research is needed in Europe and Africa on the efficacy of locally appropriate therapeutic interventions including better paediatric management of HIV, management of co-morbidities, prevention of mother to child transmission, vaccines, and microbicides. Long-term control of HIV and the development of new or improved medicinal products will require a combination of both medical innovation and development cooperation facilitated through transnational partnership.

Methods
16 European Member States and the European Commission established in 2003 the European & Developing Countries Clinical Partnership (EDCTP) to pool resources and provide a single common platform for research cooperation for European and sub-Saharan African countries in the fight against HIV, malaria and tuberculosis. EDCTP supports clinical research and capacity development activities through Calls for Proposals to develop new or improved drugs, vaccines, microbicides and diagnostics to specific and vulnerable target groups (i.e., children, pregnant women).

Results
EDCTP has awarded 246 grants corresponding to a total amount of 212€M. In total, 52 projects (21%) focused on HIV research (total grant value of 62.4M€) and most of the
funding (40€M) was allocated to HIV clinical trials (62% treatment, 31% vaccines and 7% microbicides). Other HIV research projects supported by EDCTP included immunology studies and diagnostics (total grant value of 22M€). EDCTP has funded 12 projects (4.9%) on HIV/TB co-infection with a total grant value of 7.2M€. Most EDCTP supported projects (69%) include one or more Europe-based collaborators, giving an average of four Europe-based researchers per grant. EDCTP funded HIV clinical trials have amongst others led to the registration of a paediatric formulation of an antiretroviral product (Pedimune) in Africa. In addition, a study by Prof. Bertilsson et al found no need to increase the efavirenz dose during concomitant rifampicin based anti-TB therapy in patients with HIV/TB co-infection. Results of other EDCTP supported HIV studies contributed to the development of policies both at national and international level.

**Conclusion**

Since its creation, EDCTP has created a powerful “pull” mechanism for scientists in Europe and Africa to establish or reinforce joint research programmes linked to EDCTP objectives. EDCTP has brought together a number of European countries that had no tradition of working in collaboration with Africa, ensuring synergy and optimal use of resources, and creating a win-win situation for all parties involved. EDCTP offers opportunities to conduct research that cannot be funded or delivered by a single country alone and provides a single common European platform for research cooperation with sub-Saharan Africa in the fight against HIV and other poverty related diseases. This platform will be instrumental for Baltic countries as it will facilitate engagement of national researchers in large clinical research consortia and better integration with EU research policies. The EDCTP partnership offers increased networking opportunities, including with major pharmaceutical companies and funders, and greater exposure to clinical research expertise and policy-making.
Improving vaccine immunogenicity and development of new animal models of HCV infection

Invited Abstract No 4

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Keywords

HCV, hepatitis C virus, vaccine, DNA, electroporation

Presentation type: Oral
Contact: lars.frelin@ki.se

Abstract (english) (2482 characters)

Background: The hepatitis C virus (HCV) is a major cause for chronic liver disease worldwide. Despite effective therapies it is estimated that only 10% of all chronic HCV infected individuals receive any therapy. Hence, new therapies are needed to increase the overall cure rate of HCV. One suggested treatment-regimen is therapeutic vaccination. It is well known that strong T cell responses are involved in clearance of HCV infection, whereas patients that progress to chronic HCV have severely impaired immune responses. The idea of therapeutic vaccination is to reactivate the dysfunctional HCV-specific T cell responses in the chronic carrier. We have developed and improved the immunogenicity of HCV NS3/4A-based DNA vaccines in both pre-clinical and clinical studies. One major obstacle in in vivo delivery of DNA vaccines is the transfer of the material over the membranes of the cell. To overcome this problem we have developed a new delivery technology, named In vivo Intracellular injection (IVIN) device. The combination of optimized vaccine compositions and improved delivery technologies have been evaluated in different animal models.

Method: We have developed a codon-optimized (co) HCV NS3/4A DNA vaccine (gt1a) expressed from the pVAX1 plasmid. The vaccine was delivered intramuscularly using a regular needle or the IVIN device in combination with in vivo electroporation. The NS3/4A vaccine was further optimized by addition of stork hepatitis B virus core gene sequences and co-expression of interleukin 12 (IL-12). Safety, protein expression and immunogenicity were evaluated in mice, rabbits, and pigs.

Results: Our NS3/4A-based DNA vaccine have been evaluated in two clinical trials showing that the treatment was safe and tolerable, activated HCV-specific immune responses and had transient effects on the viral load. However, therapeutic vaccination alone did not cure the HCV infected patients. Thus, we have developed new improved HCV NS3/4A-based DNA
vaccines and delivery technologies. These improvements have resulted in significantly enhanced HCV-specific immune responses compared with previously evaluated vaccines. In addition, our vaccines showed potent anti-HCV activity in an immuno-competent mouse model of HCV RNA replication.

**Conclusion:** We have shown that our optimized HCV NS3/4A vaccine in combination with IVIN delivery significantly improves the vaccine immunogenicity. Our findings support the use of NS3/4A in HCV vaccine compositions.
Vaccine developments for viral hepatitis and HIV

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Categories
VACCINES

Keywords
viral hepatitis, HIV, vaccine, development

Presentation type: Invited Oral
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Abstract (english) (597 characters)

The aim of this presentation is to make an overview of the status of HIV and HCV vaccine trials. These viruses have some replication properties in common, and for both there is now successful drug treatment (HCV) or means to convert the infection into a chronic stage (HIV). Thoughts on construction of vaccines, timing and devices for immunsations, prime-boost attempts, adjuvants for innate and adaptive immune responses, and relevant non-human primate studies will be presented, together with the possibilities to use a combination of vaccine and antiviral treatment in prophylaxis or therapy.
Hepatitis B and C - a silent epidemic

Abstract (english) (3562 characters)
Globally, an estimated 8 million new hepatitis B and C infections occur annually, and 390 million people are living with chronic hepatitis B and C; almost one million deaths are HBV-, or HCV- related. Over the last 15 years the incidence of acute hepatitis B decreased dramatically due to successful hepatitis B vaccination programs, and acute hepatitis C also occurs less often with the introduction of blood donations screening and wide awareness campaigns. Nevertheless, these two infections remain important public health issue with the majority of acute cases occurring among illicit drug users; numerous outbreaks occur in health care settings due to unsafe injections, inadequate infection control practices and narcotics diversion. Highly accurate estimates of the burden from hepatitis B and C determined by The Institute of Medicine (IOM) in its 2010 report, show that viral hepatitis is an underappreciated health concern, a silent epidemic for the United States, where 65%-75% of infected population remain unaware of their infection status. Despite the implementation of anti-HCV screening tests and other prevention strategies, every year approximately 20,000 new cases of hepatitis C occur in the United States, with 85% of them developing chronic disease. This enormous source of chronic HCV infections imposes a significant health burden. In the absence of treatment 15%-40% of persons living with viral hepatitis will develop liver cirrhosis. Rates of death related to hepatitis C in the United State rose at an average rate of 0.18 deaths per 100,000 persons per year, surpassing HIV mortality rates in 2007, when more than 15,000 people died from hepatitis. Health and Human Service (HHS) Action Plan for the Prevention, Care and Treatment of Viral Hepatitis launched in 2011, states that successful testing for HCV and better provision of care and treatment to those who are infected can decrease the burden of disease. Implementation of recommendations regarding anti-HCV screening among the 1945-1965 birth cohort- the US population with highest prevalence of HCV infection, is estimated to identify and refer to care additional 809,000 infected people,
which will help prevent 120,000 deaths from hepatitis C and avert spending of $2.5 billion in medical costs. Additional disease prevention effect is expected from massive education campaigns. In 2010, World Health Assembly approved its “Resolution 63.18: Comprehensive Hepatitis Prevention and Control”, sponsored by Brazil, Columbia and Indonesia, calling WHO to develop a comprehensive approach to hepatitis prevention and control. The Global Hepatitis Framework set the priorities for global control of viral hepatitis, especially B and C that annually silently kill almost 1 million of their victims. The Framework Axes focus on (1) development of partnership and resource mobilization, and communication; (2) accumulation of reliable data for policy and action; (3) prevention of virus transmissions; and (4) screening care and treatment. Clear understanding of hepatitis B and C epidemiology through systematic disease surveillance, and accurate identification of infected persons early in the course of disease, and referring them to care and treatment are cornerstone goals for prevention of advanced stages of liver disease and cancer. Collaborations among public health, clinical care providers, laboratories payers and industry are essential and must be implemented at the national levels, in order to stop the silent epidemic of hepatitis B and C at the global scale.
Abstract (english) (2271 characters)

Once in the middle of the eighteenth century, Edward Jenner created and applied the first vaccine against smallpox, vaccination opponents appeared. Over the next centuries the movement against vaccination was the constant companion of progress. Vaccination against hepatitis B and A is not an exception. Today anti-vaccination lobby exists all over the world including Russia. Ignorance associated with vaccination issues is reflected in television shows, in press (mainly in "tabloid" mass editions), on the Internet.

The aim of this lecture: To consider possible causes of anti-vaccination movement activation, to analyze the main arguments made against hepatitis B and A vaccination, and to observe possible strategy to combat anti-vaccination movement.

Convincing success of mass vaccination against hepatitis B and reduction of hepatitis A incidence have led to a sharp decrease in the number of severe (fatal) cases of these diseases, which gave rise to complacency society against these infections. Desire to be in the spotlight, as the saviors of mankind, from allegedly unscrupulous scientists, as well as lack of knowledge of the problem determines the nomination of anti-vaccination movement leaders. An important component in this case is an interest to press coverage of scandals attracting people's attention.

Usually such cases are based on unverified data, often distorted isolated cases. Lack of awareness about vaccination, and often simply ignorance of the population in these areas is a good background for the spread of false information. It was suggested that the hepatitis B vaccination could lead to an increase in autism, multiple sclerosis, rheumatoid arthritis, etc.
To study these assumptions numerous independent studies were held, including those led by WHO. Results of these studies deny any relationships between such disorders and vaccination against hepatitis B and A.

Today it is clear that vaccination against hepatitis B and A is the most important tool to control these infections. Successful confrontation to anti-vaccination movement requires a clear program that unites healthcare workers with different social populations. Such program should be based on an integrated approach involving evidence based effective interventions.
Increased understanding of viral spread and dynamics by the use of molecular epidemiology

Invited Abstract No 8

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**Categories**

5. Viral evolution: dynamics and geography

**Keywords**

HIV-1, molecular epidemiology, sequence analysis, phylogenetics

**Presentation type**: Oral

**Contact**: Joakim.esbjornsson@imm.ox.ac.uk

**Submission date**: 2014-03-18 15:38:49

**Abstract (English) (1600 characters)**

**Problem statement**: Increased knowledge about the determining events and factors involved in the development of new viral epidemics and subepidemics together with insights in the epidemiological dynamics of viral spread are critical for monitoring current epidemics and designing future prevention efforts.

**Methods**: Viral genetic sequences were used together with patient data in maximum-likelihood and Bayesian phylogenetic frameworks to dissect the molecular epidemiology of HIV-1 in different geographical settings.

**Results**: The current presentation will describe how to design a dataset suitable for analysis by molecular epidemiology and how such dataset can be explored by current state-of-the-art phylogenetic and phylogeographic analyses. Different datasets has been used to (1) in detail describe how epidemiologic and phylogenetic data can be combined to show how one single introduction of HIV-1 became epidemic in an isolated geographic location; (2) to show how strict phylogenetic analysis of a relatively small dataset can be used to show how and when different subtypes of HIV-1 was introduced and spread within a country; and (3) dissect the dynamics and spread of HIV-1 subtypes in different risk groups over time by the analysis of a large dataset representing >50% of all newly discovered HIV-1 infected individuals between 2000-2012 in the Scandinavian countries.

**Conclusion**: Phylogenetic analysis can increase the understanding of epidemiological dynamics, enhance surveillance-based risk information and inform national programmes for monitoring and prevention of viral infections.
Intra-Host HCV Evolution

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Categories
5. Viral evolution: dynamics and geography

Keywords
HCV, molecular evolution, sequence analysis, phylogenetics

Presentation type: Oral
Contact: ykhudyakov@cdc.gov
Submission date: 2014-03-18

Abstract (English) (1478 characters)

Hepatitis C virus (HCV) is a leading cause of chronic liver disease and hepatocellular carcinoma. Approximately 170 million people are infected with HCV worldwide, with ~3.5 million infected individuals residing in the United States, many of whom unaware of their infection status. HCV causes chronic infection in ~70% of infected persons. However, molecular mechanisms of establishing chronic infection and molecular evolution of HCV during chronic infection are not well understood. Each infection is usually established from several founders transmitted to naïve hosts from a source. HCV rapidly evolves from the founders. Intra-host HCV evolution is under control of the strengthening with time negative selection, reflecting increased adaptation of HCV to the infected host during chronic infection. The structure of intra-host HCV population is shaped by single-point mutations and variation in density of subpopulations. Immune selection plays a key role in determining the HCV genetic heterogeneity over time in infected persons. Recently, it was shown that the major neutralizing epitopes located in the hypervariable region 1 (HVR1) are extensively cross-immunoreactive, indicating that the number of immunological specificities distributed across the entire HVR1 sequence space is limited. This finding in conjunction with observation of convergence among HVR1 variants from different genotypes and subtypes points to essential restrictions on inter-host evolution.
Challenges in laboratory diagnosis of HBV and HCV infections

Authors
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Categories
IV. Diagnostics

Keywords
HCV, HBV, serology, diagnosis

Presentation type: Oral
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Submission date: 2014-03-31

Abstract (English) (2282 characters)
Serologic assays for the diagnosis of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are widely available throughout the world. The laboratory diagnostics of HBV infection is greatly facilitated by the availability of a range of serological markers which when detected alone or in combination can readily identify active infection, differentiate between acute, chronic or resolved infections as well as characterize whether the antibody responses detected is a result of vaccination or natural infection. The diagnostic landscape of HCV infection is very limited to just one antibody marker, anti-HCV IgG, which is detectable during the acute, chronic and resolved phases of infection. The diagnosis of active HCV infection is, therefore, solely based on the detection of HCV RNA by polymerase chain reaction methodologies. HCV Core antigen assay, though not widely available yet, is also used for diagnosing active HCV infection. Recent advances in molecular technologies, which include nanoparticle-based diagnostic assays, the use of aptamers as capture molecules and loop-mediated isothermal amplification assays, have produced promising new tools which have the potential for use in the development of new and improved assays for the diagnosis of HCV infection. The challenges in viral hepatitis diagnostics are posed by the many types of hepatitis viruses, all causing infections that are clinically indistinguishable and each having a multitude of viral genotypes, subtypes, and serotypes. Although well characterized and validated assays approved for clinical use by international regulatory agencies are available for markers of HBV and HCV infection, commercially available or in-house research-use-only assays are available and also being routinely used in various settings. This unregulated supply of diagnostic kits poses a challenging situation, particularly in resource-poor countries where such assays are also used for blood screening. An important step towards improving the diagnostics and also for blood safety will be to develop well characterized reference panels that can be used for evaluating the performance characteristics of all available diagnostic assays. Such panels can also be used for developing new and improved diagnostic assays.
# Principles of personified antiviral therapy for patients with chronic viral hepatitis

**Invited Abstract No 11**

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### Categories

*PATHOGENESIS AND TREATMENT*

### Keywords

viral hepatitis, antiviral therapy, personalized therapy

### Presentation type

Invited Oral

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## Abstract (english) (3 004 characters)

Hepatitis B virus and hepatitis C virus infections are widespread all over the world. Chronic course of these diseases is characterized by an increased risk of liver cirrhosis and hepatocellular carcinoma. Current treatment strategies for chronic viral hepatitis need to be improved because of the insufficient efficacy and severe side effects of antiviral therapy (AVT).

We evaluated the efficacy of personalized AVT for patients with chronic hepatitis B (CHB) and chronic hepatitis C (CHC).

Total 372 patients with CHB and CHC were followed on AVT. The study group consisted of 64 patients with HBV and 308 HCV patients (248 men, 124 women). The average age of patients was 35.8 ± 11.8 years, mean duration of observation of patients - 6.02 ± 5.33 years, including the duration of aftercare - 2.7 ± 1.2 years. In the study group 13% of patients had normal transaminase levels, in 35% - ALT levels did not exceed 2 upper level of norm (ULN), in 41% ALT levels were 2-6 times higher ULN, in 11% of patients ALT levels were > 6 ULN. ART for CHB patients included interferon (IFN) and nucleos(t)ide analogs (NA), for CHC patients - IFN and ribavirin. Treatment strategy was based on viral factors and on clinical and laboratory characteristics of chronic liver disease. Efficacy of the treatment was evaluated based on the achievement of a sustained virologic response (SVR), determined for CHC patients as absence of HCV RNA serum by polymerase chain reaction (PCR) with a sensitivity of at least 50 IU/ml for 24 weeks or more after treatment.

Efficacy of NA monotherapy in CHB patients was only 5%, whereas 14.8% patients treated with a combination of NA and IFN achieved sustained response. In this treatment group the duration of therapy was prolonged [84 weeks in averaged (SD =65 weeks)]. Treatment efficacy for CHC patients was higher compared to CHB patients and varied depending on the
IFN used (standard versus pegilated IFN) and HCV genotype. Thus, in patients with CHC treated with standard IFN and ribavirin treatment efficacy was 54.2% (in patients with genotype 1 HCV - 30%; in patients with genotypes 2 and 3 HCV - 76.6%). In patients treated with pegilated IFN and ribavirin the rates of SVR were significantly higher: 76.9% in general cohort (63.9% in patients with HCV genotype 1; 92.2 % in patients with genotypes 2 and 3 HCV). AVT efficacy depended mostly on the time of achieving the virologic response (VR). In CHC patients with VR at week 4 of treatment, the rate of SVR 89.5%, whereas in patients who achieved VR on week 5 - 12 of treatment, the rate of SVR was only 54.3%. In patients with VR after 12 weeks of treatment AVT efficacy was only 5.1%. Shortened treatment course for CHC patients with rapid SR (at week 4) did not compromise the efficacy of treatment.

Application of personified AVT in patients with chronic viral hepatitis can increase the treatment efficacy and minimize the number of side effects due to the use of SVR predictors and optimization of treatment duration.
Introduction.

Hepatitis C Virus (HCV) has emerged as a leading cause of chronic hepatitis, liver cirrhosis and hepatocellular carcinoma (HCC) worldwide. The purpose of this study was to describe the distribution pattern of HCV genotypes in chronic hepatitis patients within Campania region, an area of Southern Italy, and estimate their association with risk factors and viral load.

Material and methods.

404 consecutive HCV RNA positive patients were included in the study. HCV genotyping
Emergence of genetically variant Hepatitis C virus population in response to increased antiviral drug pressure

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Categories
1. Molecular Virology

Keywords
Hepatitis C virus, Antiviral therapy, Interferon, Ribavirin, Mutation

Presentation type: Oral
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Submission date: 2013-11-28 02:16:15

Abstract (english) (1350 characters)

Problem statement: A shift in mutation spectrum has been observed in entire HCV genome in general and in NS5B gene in particular in patients undergoing interferon (INF) plus ribavirin (RBV) therapy. However, no study is available describing genetic diversity of non-responder (NR) HCV isolates. Therefore, in the present study, we report emergent cluster of HCV-3a in patients administered with IFN plus ribavirin therapy for 24 weeks.

Methods: Total 316 HCV-3a infected patients were enrolled over a period of 1 year (January to December 2012). All the patients received standard interferon plus ribavirin treatment. Their serum samples were tested for HCV RNA at baseline, 4th week, 12-week, 24-week and 6-weeks post treatment. The entire NS5B gene was sequenced in both directions for all the HCV RNA detected samples each time.

Results: A total of 32 patient were found NR therefore there sequences were included in data analysis. Of these 22 were males and 10 were females with mean age 37.68 ±12.05 years (18 to 56 years). The HCV non-responder isolates has been classified into a distinct clad after therapy as compared to the baseline sequences.

Conclusion: The Phylogenetic classification of non-responding isolates into separate cluster suggests the emergence of distinct HCV as a result of the increased drug pressure.
was carried out by HCV LiPA test and viral load estimation by Taqman Real time PCR system.

Results.

The predominant genotype was 1 (63.6%), followed by genotype 2 (29.4%), 3 (6.2%) and 4 (0.8%). Subtype 1b was more frequent in females than in males. Conversely, genotype 3 was more frequent in males. No significant difference was observed in age distribution of HCV genotypes. Surgery and dental therapy was the most frequent risk factor for genotype 1, whereas intravenous drug abuse and tattooing for genotype 3. Patients with genotype 1 show more frequently high HCV viral load if compared to those with genotypes 2 and 3.

Conclusion.

The present study revealed that HCV genotypes 1 and 2 accounted for over 95% of all the HCV infection in Campania region and genotype 1 was associated more frequently with a higher viral load if compared to genotypes 2 and 3.
Occult hepatitis C virus infection: the Pakistan experience

Abstract No 3

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Categories
3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords
Occult hepatitis C infection, Diagnosis, RNA, Liver biopsy, False negative

Presentation type: Oral
Contact: idreeskhan96@yahoo.com
Submission date: 2013-11-28 02:22:55

Abstract (english) (2034 characters)

BACKGROUND: Occult hepatitis C infection should be considered when diagnosing patients with a liver disease of unknown etiology.

AIM: The aim of the present study was to determine the presence of HCV RNA in the liver biopsies of patients with abnormal liver tests but without detectable serum HCV RNA and anti-HCV antibodies in sera.

METHOD: Liver biopsies and whole blood of total 31 patients who were negative for anti-HCV antibodies with elevated liver function tests were received at Division of Molecular Virology National Centre of Excellence in Molecular Biology, University of the Punjab, Pakistan from January 2002 to June 2009 for the detection of HCV RNA. HCV RNA status of the subjects was tested by reverse-transcription polymerase chain reaction (RT-PCR) and quantified using SmartCycler II real-time PCR, in their liver biopsies, sera and peripheral blood mononuclear cells (PBMCs). HCV genotyping was carried out in HCV RNA positive samples using type-specific PCR.

RESULTS: HCV RNA was detected in liver-biopsy specimens from 23 (74.2%) of the total 31 patients negative for anti-HCV antibodies and undetectable serum HCV RNA. HCV RNA of both negative and positive polarity was found in the livers of 8 (25.8%) patients. Genotyping analysis showed that 65% patients were infected with HCV 3a, 17% with 3b, 13% with 1a and 4% patients were found with untypable genotype. In a multivariate logistic regression model, patients having previous history of sharing needles, presence of steatosis, elevated liver enzymes, history of previous surgeries, male sex, age above 30 years and with liver fibrosis stage F1 were significantly associated with the presence of occult HCV infection.

CONCLUSIONS: Patients with elevated liver enzymes and negative HCV antibodies and negative serum RNA may have intra-hepatic HCV RNA. The chance of occult HCV infection increases if the patient has previous history of sharing needles, elevated liver enzymes, history of previous surgeries, male sex and above 30 years of age.
HBV TRASMISSION FROM AN OCCULT CARRIER WITH FIVE MUTATIONS IN MAJOR HYDROFILIC REGION OF HBsAg TO A IMMUNOSOPPRESSED PLASMA RECIPIENT

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Categories
1. Molecular Virology

Keywords
HBV infection, occult HBV infection, transfusion, HBsAg mutants, Infected carriers

Presentation type: Oral
Contact: a.petruzziello@istitutotumori.na.it
Submission date: 2013-11-28 02:45:51

Abstract (english) (2492 characters)

A 56-year-old, Italian, male donor referred since 2008 at our Transfusion Service of Istituto Nazionale Tumori, Pascale, Naples, Italy. He had not been vaccinated against HBV, had no history of known risk factors for HBV infection. At the time of all blood donations he was negative for HBsAg and NAT determination with normal serum alanine-aminotrasferase (ALT) values. All the recipients of each blood donation remained HBsAg and HBV DNA negative also in the follow-up.
In June 25, 2010 he was again admitted at Transfusional Service for a blood donation. Since at this time he was HBsAg, anti-HCV and anti-HIV negative, negative for HBV-DNA, HCV-RNA and HIV-RNA by NAT and had normal serum ALT, the blood was transfused to three hospitalized patients. All three recipients were HBsAg negative at the time of the transfusion and had not been vaccinated against HBV; the patients 1 and 3 had a severe
immunosuppression due to the chemotherapy because of a non-Hodgkin Lymphoma. Seven months later, in January 2011, the donor came back to Transfusional Service for a new blood donation. He denied any risk factor for parenteral infection, but at this time the NAT determination was positive for HBV, although he was still HBsAg negative and had normal serum ALT. The serological study of HBV infection showed that the donor was positive for anti-HBs positive (55 IU/ml), total anti-HBc positive and anti-HBe, and negative for anti-HBc IgM and HBeAg; the serum HBV load was very low (57 IU/ml).

In order to assess the sero-virological status of the three recipients, the patients 1, 2 and 3 were recalled and tested for HBV markers. The plasma recipient (patient 1) remained HBsAg negative, but it was HBV-DNA positive (3,380 IU/ml) with abnormal serum ALT levels, confirmed in two determinations.

The platelets and red cells recipients (the patient 2 and 3, respectively) remained HBsAg and HBV-DNA negative.

The sera of the donor and of the patient n°1 were analyzed for HBV genotype and HBV pre-S/S coding region. Both had a genotype D and the HBV pre-S/S coding region sequences showed five aminoacid substitutions: T116N, T123I, D144V, G145K, I150T. In conclusion, this is a case of transmission of occult HBV infection by a plasma transfusion. Probably, the immunsoppression status of the recipient favoured the transmission and the accumulations of the five mutations in the MHR affected the reactivity of the diagnostic assay used for HBsAg.
Occult hepatitis B virus infection among Egyptian chronic hemodialysis patients.

Abstract No 5

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Categories

3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords

Occult hepatitis B virus, HBV DNA, hemodialysis, HCV, aminotransferases

Presentation type: Poster
Contact: ghadafahmy@hotmail.com
Submission date: 2013-12-20 16:10:03

Abstract (english) (2136 characters)

Background: The prevalence of end-stage renal disease has increased dramatically in developing countries. Hepatitis B virus (HBV) infection as a major global health problem represents a significant co-morbidity event that has led to several outbreaks of hepatitis B. There are inadequate data concerning occult HBV infection among Egyptian chronic hemodialysis patients (CHP). This work aimed to detect occult HBV infection among Egyptian CHP.

Methods: A cross-sectional study was performed on 100 patients with end-stage renal disease on maintenance hemodialysis and tested negative for HBV surface antigen. Blood samples were collected before initiation of hemodialysis. Sera were tested for hepatitis C virus (HCV) and Hepatitis B core (HBc) antibodies using commercially Diagnostics ELISA kits, HBV DNA by SYBR Green Real-time polymerase chain reaction (PCR) using specific primers for s and c genes, and by nested PCR using specific primers for pol gene. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities were determined by using commercially available kits.

Results: Anti-HCV and anti-HBc antibodies were detected in 34% and 48% of them respectively, 24/34(70.6%) of anti-HCV positive patients were also positive for anti-HBc
antibodies. This association was found to be statistically significant (p=0.001). HBV DNA was detected in 32% of the hemodialysis patients. A significant association was found between the presence of HBV DNA and anti-HCV positivity (p=0.021). Aminotransferases were elevated in 21% of the studied patients, notably in patients with anti-HCV positive profile than negative ones (p<0.05).

**Conclusion:** the serological markers of HBV infection should be backed up with molecular tests to investigate possible occult infections especially among anti-HBc positive hemodialysis patients for better understanding of their clinical, laboratory, and epidemiological characteristics.
Experimental model for HCV

Abstract No P6

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Categories
3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords
hepatitis C virus, flaviviridae, continuous cell lin, monolayer, polymerase chain reaction

Presentation type: Poster
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Submission date: 2014-01-13 14:29:14

Abstract (english) (2002 characters)

Background: An estimated 3 % of the world’s population are infected with hepatitis C virus (HCV). According to WHO 350 thousand people are killed by cirrhosis and hepatocellular carcinoma yearly. These chronic liver diseases are often associated with the persistent HCV infection. Extra hepatic replication of HCV is also reported. HCV is a member of the Flaviviridae family, Hepacivirus genus. The Flaviviridae family includes well-known neurotropic viruses: yellow fever virus, tick-born encephalitis virus group, dengue virus group et al.). We proposed method of HCV isolation from human blood plasma and/or sera with using cell culture.

Aim: To study the possibility of using continuous cell line the rat gasserian ganglion neurinoma (NGUK-1) for multiplication of HCV, detection of virus and RNA HCV by biomolecular method.

Methods: Serum samples from HCV-patients of clinical hospital tested by ELISA and reverse-transcriptase PCR (AmpliSense HCV-240/ICS-440). Monolayer off cells was formed during 2-3 days it depends from split ratio. A minimum volume which is sufficient the cells were set up on the formed monolayer. After incubation the serum was removed, the monolayer was washed in DMEM, and nutrient medium with 5 % fetal calf serum was added. The preparations were cultured at 37 0 C in CO2-incubator at 5 % CO2.

Results: Serum samples were positive in PCR and according to ELISA data contained specific antibodies in different levels. No cytopathic effect during cell culturing after infection. Culture fluid of the infected cells was collected after 24-96 hours and tested by real time-PCR. The levels of viral RNA was from 1200 to 252800 copies/ml. R coefficient of correlations for calibration curve was 0,99.

Conclusions: Obtained results are evidence of multiplication of HCV in the NGUK-1 cells, the confirmation of the neurotropism of HCV, the possibility of using this cell tissue culture for isolation HCV, as model to study HCV and HCV-infection.
Hepatitis mobile team: a new concept for benefit toward drugs users with hepatitis C and outside social and medical teams

Abstract No 7

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Categories

3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords

hepatitis C, drug users, inmates, hepatitis C screening, hepatitis C treatment

Presentation type: Oral
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Submission date: 2014-01-15 08:29:19

Abstract (english) (2513 characters)

Introduction: 30 to 70% of french drugs users were positive for hepatitis C but only few patients access to treatment. It was more difficult with hepatitis C tritherapy than dual therapy for drugs users to access to hepatitis screening, care and treatment. All patient need support specially psycho-educative interventions. Methods: To improve this situation we created in July 2013 hepatitis mobile team (HMT) composed hepatologist, nurse and secretary. There were 5 goals of HMT: screening of hepatitis with blood quick tests, screening of liver fibrosis with portable FIBROSCAN®, hepatology consultation directly in each unit, psycho-educative interventions and formation of social / medical staffs. All these actions were realized outside of hospital. One referent was first choosed in each drug user care unit and also in jailhouse medical unit. To complete this team, we used an psycho-educative interventions program in 2009 with specially-trained nurses outside of hospital. Program was available for all out-of-treatment patients and was free for patients who began dual therapy or tritherapy. Patients could call nurse 7/7 days; 275 patients were included in 4 years. Results: At 31th December 2013, 22 different units of Perpinya area were partners of HMT: low and high threshold methadon units, retention and detention center medical units, free meal programs, outside psychiatric units, emergency and medical hosting units… HMT became quickly helping unit to support hepatitis C patients, specially for drug users, inmates, homeless, psychiatric patients, emigrants or patients without social insurance. HMT action completed other medical
and social actions, in difficult social area. After 6 months of work outside of hospital, HMT organized 5 weekly hepatology consultations, 9 weekly or monthly nurse consultation; 92 FIBROSCAN and 99 hepatitis quick tests were realized; 4% of quicks tests were positive for hepatitis C and 12% of patients had cirrhosis or severe liver fibrosis; hepatologist saw 61 different patients and 14 patients had hepatitis C treatment with individual psycho-educative interventions; 8 collective psycho-educative interventions were also realized for total of 56 patients. Conclusions: HMT was new concept of hepatitis C care outside of hospital and doctor’s practice. It permitted screening, liver evaluation, care and treatment of difficult hepatitis patients in one specific medical or social care units, which was usual and comfortable for patients.
# Changing epidemiology and risk factors of hepatitis B in Hungary

## Abstract (english) (2010 characters)

**Background.** From 1995 to 2008, 2009 cases of acute hepatitis B were notified in Hungary resulting in 46 deaths. In 1995, the National Center for Epidemiology (NEC) started an enhanced surveillance (SYST) for acute viral hepatitis in Hungary. Starting from 1999, Hungary has universal vaccination from hepatitis B for adolescents (14 years old). We estimated the reported rates of and potential risk factors for acute HBV infection in Hungary from 1999 to 2008.

**Methods.** SYST used case definition based on clinical and serological criteria: clinical case definition and laboratory confirmation (IgM antibody to anti-HBc or HBV nucleic acid in serum). The enhanced surveillance system of viral hepatitis collects information on potential risk factors. Epidemiologists collect information on potential risk factors, including occupational exposures to blood, injection drug use (IDU), sexual behaviour, and health care exposures. We estimated the reported hepatitis B rates over 10 years period giving annual reported incidence (per 100,000 population) and we calculated the proportions of reported exposures among cases.

**Results.** Reported acute hepatitis B rates remained stable in 1999-2005 (average, 1.1 cases per 100,000 population). In 2006-2008, rates dropped below 1.0 case per 100,000 population. From 1999 to 2008, epidemiological information available for 93% of cases indicated that 51% of cases did not report any potential risk factors. Anti-HBc IgM to be positive for 839 out of 1161 reported cases. The median age of those increased from 35 years in 1999 to 42 years in 2007. The proportion of cases reporting healthcare exposure increased from 30% in 1999 to 38% in 2008.

**Conclusions.** Hepatitis B rates decreased from with an increase in (1) age of infection (2) the proportion of cases reporting health care exposures. We recommended analytical
epidemiological investigations to assess the relative contributions of medical interventions and sexual behaviour in HBV transmission.
In vivo evaluation of the efficacy of intradermal and intramuscular gene vaccine delivery

Abstract No 9

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Categories
5. Vaccine Development

Keywords
DNA vaccine, in vivo imaging, delivery, electroporation

Presentation type: Poster
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Submission date: 2014-03-24 07:23:01

Abstract (english) (2501 characters)

BACKGROUND The development of DNA vaccines strongly depends on the methods used for their delivery. Electroporation (EP) is one of the most efficient gene delivery techniques. It grossly enhances gene expression promoting a strong immune response. Studies have revealed the importance of a precise control of gene delivery. Here, we investigated how the choice of injection site and EP conditions influences DNA-vaccine expression and immunogenicity in BALB/c mice, using as a model a firefly luciferase gene (Luc).

METHODS Immunization was monitored by visualizing the in vivo expression of luciferase (Luc) by 2D- and 3D-bioluminescence imaging (BLI) and by the end-point immunoassays. Anti-Luc antibodies were assessed by ELISA, and T cell response by IFN-γ and IL-2 Fluorospot in which mouse splenocytes were stimulated with Luc or a peptide representing its immunodominant CD8+ T-cell epitope GFQSMYTFV.

RESULTS Model gene injections with subsequent EP monitored by BLI identified the parameters promoting the highest gene expression. Intradermal needle injection of Luc gene followed by optimal EP led to a low level Luc expression in mouse skin and triggered a CD8+ T-cell response characterized by GFQSMYTFV-specific secretion of IFN-γ and IL-2, but failed to induce specific antibodies. Intramuscular needle delivery of Luc gene followed by optimal EP resulted in a several-fold higher Luc expression, but induced low IL-2 and virtually no specific IFN-γ secretion. Total photon flux from the site of id Luc gene injection was inversely proportional to the immune response against GFQSMYTFV (p<0.05). The induction of T-cell response could be predicted from the time span required for the total photon flux to decrease to ≤10% of the flux registered at the injection site by day 9 after
CONCLUSIONS This study demonstrates the critical role of the site of DNA vaccination for the type and magnitude of vaccine-specific immune response. Our results indicate that skin is the tissue of choice to induce potent T-cell responses, and that such responses can be efficiently raised even by weak immunogens. Further, we demonstrate that BLI permits to control the accuracy of gene injection and EP-driven in vivo transfection. The use of luminescent reporters in preclinical gene vaccine tests can significantly diminish the animal use and the number of immune tests to be performed in preclinical testing of purely genetic or vectorized vaccines.
The HIV-1 subtypes in Belarus, 2013

Abstract No P10

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Categories

1. Molecular Virology

Keywords

HIV, subtypes, sequencing, epidemiology

Presentation type: Poster

Contact: veremin@mail.ru

Submission date: 2014-02-11 05:01:11

Abstract (english) (2493 characters)

Background. In the present in Republic of Belarus steadily high gain of new cases of HIV infection is observed. For January 1st, 2014 in the country 15711 cases HIV/AIDS whereas for January 1, 2013 14178 HIV-infected were revealed are officially registered. In the present theses we provide data on the subtypes characteristic of HIV-1 at initially revealed HIV/AIDS patients in Belarus during 2013.

Materials and methods. ELISA (Ag/Ab), Western blot, RT-PCR, ViroSeq HIV-1 Genotyping System v.2.0. Sequencing Analysis v5.1.1 programs. SeqScape v.2.6, BioEdit software. Phylogenetic trees built with MEGA4.1 program application (neighbor-joining method).

Results. 52 RNA samples of HIV/AIDS patients on gag gene (p17/p24 region) have been sequenced: 15 from the Grodno region (Grodno, Lida and Slonim), 9 from Mogilyov (Mogilyov and Osipovichi), 6 from Minsk and 16 from the Minsk region (Soligorsk and Logoysk), on 3 samples from the Brest and Gomel oblast. 52 RNA samples have been sequenced on env gene (V3 gp120 loop region): 5 samples were from the Grodno region (Grodno and Leda), 16 from the Mogilyov oblast (Mogilyov and Osipovichi), 3 from Minsk, 15 from the Minsk region (Soligorsk and Logosk), 7 from the Brest region (Brest, Pinsk and Baranovichi), 5 samples from the Vitebsk and 1 sample from the Gomel region. On a pol gene 76 RNA specimens (46 from males, and 30 – female) have been sequenced. 17 samples from Minsk, from the Minsk region –33, from Gomel – 10, from Vitebsk – 5, from Brest – 7, from Mogilyov - 4. The age of patients fluctuated from 1 year to 84 years. The carried-out phylogenetic analysis showed that on gag gene 43 (82.7%) sample were A1, 4 (7.7%) - CRF03_AB, 2 (3.8%) - subtype B, on 1 (1.9%) to subtypes G and CRF06_cpx, CRF02_AG and URF. On env gene (gp120 V3 loop) 41 (78.8%) were subtype A1, 3 (5.8%) -subtype B, 5
(9.6%) - CRF03_AB on 1 (1.9%) to a subtype G, CRF06_cpx and CRF02_AG. All samples, sequenced on gene pol region belonged to the HIV A1 subtype.

Conclusion. Thus it is shown that in the territory of Belarus the HIV-1 subtype A1 of which more than 85% of all new cases of infection are the share continues to dominate. At the same time, the quantity of recombinant forms of which more than 6% of new cases of infection already are the share increases. For the first time in the Gomel region at two patients HIV-1 subtype G is revealed, is shown that both patients got a virus from one source.
# HBV genotypes/subtypes in Belarus

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## Categories
3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

## Keywords
HBV, virus, genotypes, subtypes, sequencing

### Abstract (english) (1998 characters)

**Background.** In the last some years in the republic increase in quantity of cases of chronic hepatitis B is observed. So, if in 2010 there were 457 cases, in 2012 already 753 new cases of chronic hepatitis B were registered.

**Materials and methods.** 351 samples of blood serum/plasma from patients (202 male and 149 female) from different regions of Belarus were sequenced. The age of patients fluctuated from 6 months to 75 years. All samples were HBsAg and HBV DNA positive. Genotyping was carried out on gene P region (reverse transcriptase), a 750 bp HBV DNA fragment was analyzed. Following programs were used for analysis: sequencing analysis, v.5.1.1. SeqScape v.2.6, BioEdit; phylogenetic analysis, MEGA 4.1.

**Results.** In 290 (82.6±3.2%) samples HBV D genotype was defined. The genotype A was revealed in 55 (15.7 ± 3.9%), C in 5 (1.4 ±3.1%) samples. The carried-out phylogenetic analysis of the sequences received DNA fragments allowed to establish that all isolates of a genotype A belonged to the A2 subtype, and a genotype C – to the HBV C2 subtype. Thus all samples with a HBV A genotype were obtained from inhabitants of Belarus, and the genotype C was defined in citizens of Vietnam and China who has arrived to work in our country. Among samples with a HBV D genotype all known 4 subtypes were revealed: D1, D2, D3 and D4. 129 patients (44.5%) of all cases HBV D genotype, were carriers D2 subtype. In 88 (30.3%) cases HBV D3 subtype was defined. The D1 and D4 subtypes were defined in 69 (23.8%) and 4 (1.4%) samples, respectively. For the first time in the Republic at the patient
from Vietnam HBV B4 subtype was defined.

**Conclusion.** Thus, as showed the conducted researches in Belarus among patients with chronic hepatitis B the D (D1, D2, D3, D4) HBV genotype demanding expensive combined therapy dominates. Thus it should be noted that population of a virus of subtype D heterogeneous that indicates different sources and ways of virus penetration on the territory of the country.
HIV DRUG RESISTANCE AT PATIENTS ON HAART IN BELARUS

Abstract No P12

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Categories

8. Post- and pre-exposure prophylaxis

Keywords

HIV, subtypes, HAART, resistance, mutations

Presentation type: Poster
Contact: veremin@mail.ru
Submission date: 2014-02-11 05:43:01

Abstract (english) (2562 characters)

Background. Currently, in Belarus more than 5000 patients are on HAART, while in year 2008 only 1,200 patients were receiving this therapy, in year 2004 - only 15 patients. It is planned, that by the year 2015 - 7,000 patients will be on ART.

Materials and methods. 59 (adults) HIV/AIDS patients who have been on HAART during the period from year 2008 to year 2013. ELISA, Western blot, RT-PCR, sequencing.

«Sequencing Analysis Software v.5.1.1», «BioEdit», «SeqScape v.2.6», MEGA 4.1 software.

Results. Of the 59 patients (adults) who have been identified to have a virus with a high level resistance to HAART drugs, there were 39 male (median age 37.2 ± 4.8 years) and 20 female (median age 33.9 ± 4.92 years). 20 patients (6 male and 14 female) were infected heterosexually and 39 (33 male and 6 female) were IDUs. 55 (93.2%) patients were identified as carriers of human subtype A HIV-1, 3 (6%) were infected with recombinant forms of CRF06_cpx and CRF03_AB and one patient (2%) was infected with subtype B. In 38 (64.4%) patients (24 male and 14 female) mutation M184V/I was identified, which causes high level HIV resistance to NRTIs. In 27 (45.8%) patients (13 female and 14 male) K103N mutation was detected, which determines high level HIV resistance to NNRTIs. In 20 (33.9%) patients (16 male and 4 female) we found G190G/S/A mutation, which is associated with the emergence of high-level resistance mutations to NNRTIs. In 11 (18.6%) and 8 (13.6%) patients were identified to have T215F and K70R mutations, which determine reduction in susceptibility to AZT, d4T and ADC, as well as AZT, d4T and TDF, respectively. In 15
(25.4%) patients (3 female and 12 male) we detected a combination of mutations M184V + G190S. In 11 (18.6%) HIV infected patients (6 female and 5 male) was detected combination of resistance mutations K103N + M184V. More often, in 49.2% of cases (29 people), high-level resistance mutations were detected in patients who have the disease experience of 10 or more years.

Conclusion(s). Thus, timely, early-stage identification of HIV/AIDS infection and prompt prescription and provision of the patient with most efficient antiretroviral drug therapy schemes will substantially improve quality of our help to this category of patients. Most frequently mutations were detected in patients after 2-4 years of treatment. For example, in 45 (76.3%) adult patients and 8 (50%) children high-level resistance mutations were detected after 2-4 years of taking ART.
Analysis of transmitted HIV-1 variants among acutely infected people who inject drugs in Saint Petersburg reveals the HIV-1 transmission bottleneck

Abstract No 13

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Categories
1. Molecular Virology

Keywords
HIV diversity, transmitted virus, Injection drug users

Presentation type : Oral
Contact : contact@biomed.spb.ru
Submission date : 2014-02-27 12:46:57
Jury validation date : 0000-00-00 00:00:00

Abstract (english) (2078 characters)

Background: The expansion of the HIV-1 epidemic in Russia is mostly among people who inject drugs (PWID) due to unsafe injection practices with parenteral transmission. A pilot study to determine the feasibility of detecting acute HIV infection in PWID in St. Petersburg, Russia was conducted in 2011. Here we report the results of the molecular analysis of longitudinal blood samples obtained from the acutely infected IDUs and their risk network partners.

Methods: We performed phylogenetic analysis of the SGA-derived full-length env genes of acutely infected IDUs to estimate the multiplicity of HIV-1 infection. The AHI participants...
were also followed for up to 12 months with the weekly blood draws in the first month post-infection. We included single blood samples of the network members into the analysis to determine possible in-network transmission events. We analyzed the behavioral data provided by the subjects to suggest the parenteral over sexual transmission.

Results: We obtained single env genes for 32 cDNAs samples from the blood of 7 AHI subjects and 8 members of their risk network. All sequences represented region-specific subtype A strains. We identified 3 potential transmission clusters: two included the chronically infected subject, and one was an AHI-to-AHI case. For all of the AHI subjects including those who were suggested to have predominantly injection risk of HIV-1 acquisition we confirmed that a single variant established each HIV-1 infection. We detected superinfection and subsequent recombination of the diverse strains in one subject. Combining these data with our previously described findings, we have found that in 14 out of 19 (74%) IDU cases HIV-1 infection was initiated by the single viral variant.

Conclusions: Similar to the sexual route of infection, injection drug use in St. Petersburg, Russia, is associated with single-variant HIV transmission. High HIV-1 incidence and prevalence, low genetic diversity and a transmission bottleneck make this population a good candidate for preventive HIV-1 vaccine trials.
Correlation between HBsAg level and viral load in pregnant women

Abstract No 14

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Categories

3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords

HBsAg level, viral load, pregnant women

Presentation type: Oral

Contact: belopolskaya.maria@yahoo.com

Submission date: 2014-03-03 11:37:49

Abstract (english) (1578 characters)

Background and aims:
Viral load is one of the main markers used to diagnose hepatitis B and to determine its phase. The load’s measurement is necessary to estimate mother-to-child transmission risk for women with chronic hepatitis B (CHB). However, this method is expensive. Recently, HBsAg serum level with serum HBV DNA have been used as a marker to monitor patients with CHB. The dependency between these two markers is still insufficiently investigated. Hence, the present study was done to determine the correlation between HBV DNA level and quantity of HBsAg in different group patients.

Materials and methods:
3 groups of CHB patients were considered: pregnant women (n=25), non-pregnant women (n=19) and men (n=30). Patients with co-infection HCV, HDV and HIV were excluded. At the time of the measurement none of the patients was receiving any antiviral treatment. HBV DNA was measured by real-time polymerase chain reaction (PCR). Serum HBsAg level was measured by Architect HBsAg. Dependency between viral load and HBsAg level was determined by the Spearman correlation ρ.

Results:
In the all groups the correlation between HBsAg serum level and HBV DNA level is significant: pregnant women (mean age 28.36) – ρ=0.559, P<0.01, non-pregnant women (mean age 42.78) – ρ=0.582, P<0.01 and men (mean age 37.6) – ρ=0.439, P<0.05.

Conclusions:
Serum HBsAg level correlates with HBV DNA in patients with CHB, especially for the
women, so HBsAg levels can be used to predict a high viral load, in particular for pregnant women.
Asymptomatic hepatitis C prevalence in anti-HCV positive subjects (population based study).

Abstract (english) (1738 characters)

Aim. To determine asymptomatic HCV carriers during screening study of voluntary subjects for anti-HCV prevalence in Lithuania.

Methods. The volunteers who wanted to know their anti-HCV status in Vilnius, Kaunas, Klaipeda, Panevezys, Siauliai, Ignalina, Utena and Zarasai regions of Lithuania were admitted for the anonymous testing. Screening for anti-HCV was performed on the peripheral capillary blood using rapid lateral flow immunochromatography test (Core HCV-WB). All anti-HCV-positive subjects were confirmed on the serum samples with 2-step chemiluminescent microparticle immunoassay (Architect System anti-HCV; Abbott). Confirmed cases were tested on HCV RNR with COBAS AMPLICOR Hepatitis C Virus (HCV) Test, version 2.0. HCV genotyping was performed using VERSANT HCV Genotyping 2.0 assay (LiPA).
Results. Overall 3566 subjects were voluntary tested from the different regions of Lithuania and 85/2.4% were found anti-HCV positive according to the screening test results. Among them 34 refused further testing while 51/60% were tested for anti-HCV confirmation and out of them 44/86,3% were found anti-HCV positive on serum testing. Based on this results we can predict that 2,1% of Lithuanian population is anti-HCV positive. From 44 anti-HCV positive cases in 29/65.9% HCV RNA in serum was found, 15/34.1% were HCV RNA negative. All HCV RNA positive subjects had no evident hepatitis symptoms. In 13/45% positive subjects HCV genotype 1 was found, in 6/20% - HCV genotype 2 and in 10/35% genotype 3.

Conclusions. The prevalence of anti-HCV according to confirmation test results is 2.1%. 65.9% of anti-HCV positive cases were found being asymptomatic HCV carriers. Among them HCV genotype 1 was mostly prevailed.
The diagnostic potential of the GeneXpert MTB/RIF® test in early and fast diagnosis of pulmonary tuberculosis among high risk people in Vilnius, Lithuania

Abstract No P16

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Categories
3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords
pulmonary tuberculosis , high risk people , GeneXpert MTB/RIF® test

Presentation type: Poster
Contact: virga.macioniene@gmail.com
Submission date: 2014-03-12 11:18:24

Abstract (english) (2309 characters)

Background: Tuberculosis (TB) case rates are increasing worldwide. Lithuania is classified as medium increase countries, where patients are 25-100 cases per 100000 of population. A diagnosis of TB is a sentinel event representing recent transmission Mycobacterium tuberculosis in the community. TB epidemiological situation is difficult due to the unstable socio-economics status, unemployment, the excessive alcohol consumption.

Design: Retrospective, selective, instantaneous study was performed at a temporary stay houses and Vilnius Caritas charity canteen in December 2012.

Objective: The aim of the present study was to detect early and fast pulmonary TB among interviewed persons, to assess the risk of the spread of TB, to describe demographic, social and dependences persons without permanent residence.

Methods: In 1 month persons without permanent residence, who suffered from persistent fever or cough, or sputum production and agreed to be tested and, if necessary, treated for TB were investigated. 150 persons were interviewed, but only 40 subjects included to the study. 40 sputum samples were obtained and analyzed using the GeneXpert MTB/RIF® without knowing the final diagnosis of the subjects.

Results: The majority of subjects were male (88.8%). Breakdown by ethnicity reflects the normal distribution of the nationalities living in Lithuania. 60% of study subjects were people of working age. Even 91.5 % respondents were without passing. 77.5 % surveyed individuals had secondary or higher education. 45 % respondents did not have a home more than 10 years. During one year about 60 % subjects visited out-patient departments and 30 % were treated in the hospital. Distribution according the dependences of men was 89 %, only 11.1 % of women. The main risk TB risk factors included: cough - 80 %, sputum - 47.7 %, TB
environment 47.5%, TB in the past 25%. 2 sputum samples were positive, which accounts for 5% of study population. To both patients TB diagnosis was approved by isolation M. tuberculosis by culture from sputum and successfully treated.

Conclusions: TB early and fast diagnosis among people with social problems and without permanent residence is highly important to prevent transition of TB in the community. The men are becoming more socially vulnerable.
Self-reported cases of sexually transmitted infections in Lithuanian men having sex with men as compared to neighbouring countries (Latvia, Estonia, Poland)

Abstract No P17

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Categories

3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords

MSM, self-reporting, HIV, internet survey, STI

Presentation type: Poster

Contact: ulac@ulac.lt

Submission date: 2014-03-19 15:04:43

Abstract (english) (2507 characters)

Problem statement. Sexually transmitted infections including HIV remain, worldwide, a major public health problem. Although populations most at risk vary across countries, it is recognised that in the countries of the European Union and the European Economic Area (EU/EEA) men who have sex with men (MSM) are disproportionately affected by HIV and other sexually transmitted infections (STI).

Methods. In 2010 over 180 000 MSM across Europe – from totally 38 countries participated in the European Men who have sex with men Internet Survey (EMIS) and completed an online questionnaire in one of 25 languages. The questionnaire, among others, included questions about HIV and STI testing and diagnoses. Self-reported prevalence of STI and HIV in Lithuania and neighbouring countries (Latvia, Estonia, Poland) was evaluated and compared.

Results. 2% of respondents in Lithuania reported to be HIV positive (total number 595, age median 27 years, age median of 27 EU countries 31 years), 1.7% in Estonia (total number 612, age median 30 years), 3.9% in Latvia (total number 734, age median 30 years), 5.1% in Poland (total number 2873, age median 28 years). This percentage means estimated HIV prevalence, the EU27 median is 5.1%. Diagnosed with STI other than HIV in previous 12 months: 3.6%, 13.5%, 4%, and 7.1% respectively, EU27 median 7.2%. Diagnosed with
syphilis in previous 12 months: 0.2%, 0.7%, 1%, 2.1% respectively, EU27 median 1.9%. Diagnosed with gonorrhea in previous 12 months: 1.2%, 1%, 1.2%, and 1.7% respectively, EU27 median 1.8%. Diagnosed with chlamydia in previous 12 months: 0.5, 1.4%, 1.1%, and 0.8% respectively, EU27 median 1.4%. First diagnosed with anal or genital herpes in previous 12 months: 0.3%, 0%, 0.7% and 1.1% respectively, EU27 median 0.7%. First diagnosed with anal or genital warts in previous 12 months: 1.7%, 1.2%, 1%, and 2.4% respectively, EU27 median 2.5%. Diagnosed with hepatitis C (MSM with HIV without injecting drug use): 11.8%, no data from Estonia, 6.1% in Latvia, and 1.4% in Poland, EU27 median 5.8%. Conclusion. Estimated HIV prevalence in Estonia, Latvia and Lithuania was lower as EU median, in Poland equaled the EU median. Estimated prevalence of other STI was, generally, also lower. Estimated syphilis prevalence in Poland was higher as EU median. Percentage of the self-reported diagnosis with hepatitis C in Lithuania was twice as high as EU median, ninefold higher as in Poland and almost twofold higher as in Latvia.
Sexual risk behaviour among men who have sex with men in Lithuania, results of the EMIS survey

Abstract No P18

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Categories

3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords

MSM, internet survey, risk-taking behaviour

Presentation type: Poster
Contact: ulac@ulac.lt
Submission date: 2014-03-18 13:00:41

Abstract (english) (2459 characters)

Problem statement. Men who have sex with men (MSM) remain one of the groups most at risk of HIV. Although risk reduction interventions are being widely reported, these appear to offer limited protection to HIV-negative MSM. There has been resurgence in diagnosed HIV infections noted among MSM populations in Western Europe in recent years. MSM who use substances are more likely to engage in sexual risk behavior.

Methods. In 2010 the internet survey of MSM (EMIS) has been performed in 38 European countries by applying the online questionnaire, which sought 278 data items. One of the survey focus areas was identification of sexual risk behavior among MSM.

Results. The major focus of the analyses was to gain insight into levels of unprotected anal intercourse (UAI), which is attributed to the highest risk-taking behaviour in regard of HIV infection. 60.6% of the respondents had had any UAI with a man in previous 12 months. 71.7% reported having sex with steady partner in previous 12 months. 70.3% of them did not use condoms while having sex with steady partner and 38% had had UAI with a steady partner of unknown or discordant HIV status in previous 12 months. 11% of the respondents had had more than 10 non-steady partners, 42.4% reported any UAI with a non-steady partner in last year. 27.1% had had UAI with non-steady partner of unknown or discordant HIV status in the last year.

39.8% reported UAI with any male partner in the previous 12 months. 18.1% admitted to have had sex abroad in previous 12 months, of them 54.2% had anal intercourse during the last episode of sex abroad, and of those 17.3% had UAI. 7.3% of the respondents reported paying for sex, and 40% of those had paid a man for sex more than 10 times in previous 12 months. 5.3% reported having been paid for sex in previous 12 months, of them 19.2% have been paid for sex more than 10 times. 3.2% had had paid for sex and 5.3% had been paid for
sex while traveling abroad in previous 12 months. Study of substance abuse resulted in the following observations. 2.9% of the respondents reported history of self-injection, 42.9% had used alcohol daily, of them 18.7% were concerned about their use of alcohol. Only 2.2% were concerned about their use of recreational drugs.

Conclusion. MSM in Lithuania, according to the self-reporting, often engage into risky behaviour, and reducing HIV transmission in this population group remains a significant challenge.
Identifying the Main Determinants of the Spread of the 2009 H1N1 Influenza Pandemic in Europe

Abstract (english) (2099 characters)

The 2009 H1N1 influenza pandemic spread very quickly across the globe but in a highly heterogeneous way. A notable pattern occurred in Europe, with the UK exhibiting a first wave in early summer and a second wave in autumn, while all other European countries experienced a single wave in autumn/winter. Moreover, a clear West to East pattern of spread has been observed.

We make use of a large-scale microsimulation model informed with social and demographic data coming from 37 European countries and parameterized on the basis of epidemiological data on the H1N1pdm strain available by the beginning of June 2009 to investigate the spatiotemporal dynamics of the pandemic and to identify the main factors determining its spread across Europe.

The model provides a description of pandemic spread through Europe, depending on intra-European mobility patterns and socio-demographic structure of the European populations, which is in broad agreement with observed timing of the pandemic in different countries. Attack rates are predicted to depend on the socio-demographic structure, with age dependent attack rates broadly agreeing with available serological data. Results suggest that the observed heterogeneity can be partly explained by the between-country differences in Europe: marked differences in school calendars, mobility patterns and sociodemographic structures. Moreover, higher susceptibility of children to infection played a key role in determining the epidemiology of the 2009 pandemic. Notably, we show that, differently from Western European countries that are characterized by high fluxes of travel from/to the US, intra-European mobility was crucial to determine the timing of spread in Northern and Eastern
European countries.

Our work gives rather clear expectations as to the likely impact and spatiotemporal dynamics of the pandemic, and highlights that it would have been possible to obtain a broad-brush prediction of timing of the European pandemic well before the autumn of 2009, reducing uncertainty and improving situational awareness for policy makers across Europe.
Optimization of chimeric Hepatitis B virus core particles bearing fragments of Hepatitis C virus non-structural protein 3

Abstract (english) (1535 characters)

Hepatitis C virus (HCV) persists in up to 85% of infected individuals as a chronic infection characterized by liver infiltration of inflammatory cells that can lead to fibrosis, cirrhosis and hepatocellular carcinoma. Chronic HCV infection results from weak or absent T cell responses. Pegulated-interferon-alpha (INF-α) and ribavirin, the standart of care for chronic HCV, have numerous immune effects but are not potent T cell activators. A potent immune activator such as TLR9 agonist CpG deoxyoligonucleotide (CpG) may help current treatment approaches. It was shown that vigorous T helper and cytotoxic T cell response to nonstructural protein 3 (NS3) of HCV plays significant role in the clearance of the virus. Therefore the aim of this study was to create unique type of HCV immunogen capable of induction of specific HCV cellular immune response. Chimeric virus-like particles bearing different NS3 regions, containing several CD4+ and
CD8+ epitopes, were created on the basis of hepatitis B virus core protein (HBc). To enhance the immunogenicity of these chimeric capsids, immunostimulatory CpG oligonucleotides were packaged into the particles. Furthermore to facilitate uptake of prototype vaccine into dendritic cells well known as major antigen presenting cells, RGD tripeptide will be introduced into constructs. RGD tripeptide was shown to bind to α-integrins which are commonly expressed on the surface of dendritic cells. Such type of HCV immunogen could serve as effective vaccine candidate.
Improving of vaccine prototypes on the basis of the HCV core

Abstract No P21

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Categories

5. Vaccine Development

Keywords

HCV core, vaccine, ARFP

Presentation type: Poster

Contact: irina@biomed.lu.lv

Submission date: 2014-03-21 08:47:13

Abstract (english) (1486 characters)

To employ HCV core as an attractive component of HCV vaccine, we plan to improve its immunogenicity. The objective of this study consists in the elucidation of the molecular mechanisms behind peculiar HCV core immunogenic performance and its involvement into design of improved HCV core-based DNA immunogens, in order to develop them into “equal partners” or “first line players” compared to other HCV antigens. HCV core protein sequence can also mediate the synthesis of the F protein which is synthesized as a result of a ribosomal frameshift. The F protein may participate in HCV morphology or replication. F protein has potential value in diagnostic tests and as a component of vaccines. The central aim of the study is to clarify the impact of protein F on the the structural, functional, and immunological properties of genetic vaccines based of HCV core. A set of eukaryotic expression plasmids containing wt variant of HCV core, version of core wt with prohibited ARFP expression and construct exclusively expressing ARFP was generated. Plasmids on the basis of HCV cores and its ARFPs were designed according to FDA recommendations, which approve appropriate constructs for human use. The properties
of obtained expression constructs will be studied in the immunization experiments on the Balb/c mice. For testing of DNA-immunized animals’ sera we going to use different variants of purified HCV core and ARFP proteins expressed in E.coli cells.
HIV-1 molecular epidemiology in Lithuania

Abstract (english) (2509 characters)

Problem statement. HIV epidemic in Lithuania and neighbouring countries primarily affects injecting drug users (IDUs) and their sexual partners. In 2008 Lithuania remained among the least affected countries, with the total number of registered HIV-1 infections of 1,200 (0.1% of population). No molecular-epidemiological studies have been carried out in Lithuania up to 2008, when this study of HIV-1 genotypes circulating in Lithuania and transmission of drug-resistant viruses was performed.

Methods. Clinical samples (plasma or serum) and epidemiological information were obtained from 138 HIV-1-infected residents, which was >11% of the total infected population. Both the proportion of IDUs (n=77), heterosexually-infected (n=33), MSM (n=21), unknown transmission way (n=7) in this study and the proportion of males correspond to their proportion in the total infected population. 27 individuals were newly infected in 2008 (10 IDUs, 9 heterosexuals, 5 MSM, 3 unknown way). Phylogenetic analysis and analysis of virus genotypes were performed.

Results. Phylogenetic analysis demonstrated a remarkable variety of viruses: subtype A strains were found in 60% of individuals, followed by subtype B (22%) and CRF03_AB (12%) strains. The remaining 7% of strains included variants belonging to subtype C, CRF01_AE, CRF02_AG, more complex recombinant forms, and strains that could not be reliably genotyped. Analysis of virus genotypes per risk group revealed circulation of distinct HIV-1 strains in different risk groups: subtype A viruses were present in 82% of injecting drug users (IDUs), but less than a half of heterosexually-infected individuals and cases with unknown transmission route, and none of men having sex with men (MSM). No mutations causing drug resistance among 27 newly diagnosed with HIV-1 cases were observed.
Conclusion. HIV-1 epidemic in Lithuania was caused by a variety of circulating HIV-1 genotypes with distinct HIV-1 strains circulating in different risk groups. IDUs and MSM represented two separate epidemiological networks, despite the geographical and likely behavioral overlap of these populations. Lithuania appeared to be the only country in which CRF03_AB viruses are epidemiologically significant, in addition to the bordering Russian enclave of Kaliningrad region. The absence of transmitted drug-resistant strains might be explained by the late onset of the epidemic, when patients were initially and properly treated by potent antiretroviral regimens.
The immune correlates of the DNA-vaccine against HIV-1 “DNA-4” identified during clinical trial.

Abstract (english) (2554 characters)

Background and aims. Identifying correlates of protection remains one of the most important points providing the key to understand how immune responses are relevant to protection against HIV acquisition. In this study we assessed specific immune responses induced in healthy HIV-1 uninfected adults by the vaccination with candidate DNA-vaccine against HIV. We also compared them with immune responses observed in highly exposed seronegative (ESN) individuals to figure out the possible immune correlates.

Methods. 21 participants of the 1st phase of «DNA-4» vaccine clinical trial, 9 seronegative injection drug users (IDUs), 10 seronegative individuals and 9 their HIV-positive sexual and/or IDU partners from the cohort of IDUs were included in the study. Trial participants received 0.25 or 0.5 or 1.0 mg of DNA-4 at days 0, 6, 10 and 14. Detection of HIV-1 specific cellular responses was performed using the IFN-γ ELISPOT assay and Intracellular cytokine staining after stimulation with HIV peptide pools (Nef, Gag, RT, Env).
Results. 17 out of 19 (89%) seronegative study subjects had strong Nef peptide pool specific cellular immune responses, 4 (21%) subjects responded against Gag peptide pool, and 1 subject had RT peptide pool response. All HIV-positive subjects had strong cellular responses against all four peptide pools. The functional profiles of the immune responses were different between the ESN group and the HIV-positive group. In ESN group we observed increased level of TNFα expression by CD4+ T-cells after the stimulation with Nef protein. And number of polyspecific T-cells was also increased.

"DNA-4" causes the formation of CD4+ and CD8+ T cells expressing cytokines in response to specific peptide stimulation, as well as polyspecific T-lymphocytes. And it may be noted that the number of T cells expressing TNFα was increased among CD4+ cells. Number of polyspecific lymphocytes was higher among cytotoxic T cells.

Conclusions. We observed high rate of specific immune responses in ESN individuals. We could assume that observed responses were induced by the infection of the cells with HIV-1. It means that this T-cellular response is probably protective. Moreover, immune responses induced in healthy clinical trial participants by DNA vaccination were similar to responses discovered in ESN individuals. So increased TNFα expression by CD4+ T-cells in response to the specific stimulation is probably one of the immune correlate of the effective HIV vaccine.
Evaluation of a hepatitis C virus therapeutic vaccine candidate in wildtype- and HCV-transgenic mice.

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Categories

5. Vaccine Development

Keywords

hepatitis C virus, genetic vaccine, vaccine delivery, animal models, NS5A

Presentation type : Oral
Contact : fredrik.holmstrom@ki.se
Submission date : 2014-03-19 22:32:59

Abstract (english) (1797 characters)

Background: The non-structural 5A (NS5A) protein of hepatitis C virus (HCV) is an essential component of the HCV replication complex. It has been shown that patients resolving chronic HCV infection have NS5A-specific T cells. Our NS5A-based DNA vaccine has been evaluated in wildtype- and HCV-transgenic (Tg) mouse models. Also, the vaccine efficiency has been improved by an optimized delivery system “in vivo intracellular injection device” (IVIN) and the addition of non-HCV gene sequences.

Methods: A codon-optimized (co) NS5A gene (genotype 1b) was cloned and expressed from a eukaryotic expression plasmid. The vaccine was delivered intramuscularly in combination with in vivo electroporation. The coNS5A vaccine was further optimized by addition of stork hepatitis B virus core gene sequences (cosHBcAg) and delivered using the IVIN technology.

Result: Our data show that 50μg coNS5A is the lowest dose needed to prime strong IFNγ- and IL-2-production in wildtype- and NS5A-Tg mice. In CD4- and CD8-deficient mice weak or undetectable immune responses were detected. Importantly, high frequencies of NS5A-specific CD8+ T cells could be primed by one single immunization in wildtype- and NS5A-Tg mice, which could inhibit growth of in vivo tumors expressing NS5A. Interestingly, our second-generation vaccine (coNS5A-cosHBcAg) primed significantly stronger NS5A-specific immune responses compared to the coNS5A vaccine in wildtype-, NS5A-Tg and HLA-A2-Tg-mice. Importantly, both frequency and magnitude of the activated immune responses were
improved.

**Conclusion:** We have shown that our second-generation NS5A-DNA vaccine is superior the coNS5A in priming NS5A-specific T cell responses. Thus, the coNS5A-cosHBeAg-vaccine is a promising therapeutic vaccine candidate.
Hepatitis E virus infection in Estonia

Abstract (english) (2467 characters)

**Background and aims:** Food- and waterborne transmission of hepatitis E virus (HEV) is recognized as an important public health issue due to globalization of food markets and the increasing number of travels into HEV endemic countries. Accumulating evidence indicated that hepatitis E is a zoonotic disease, and swine and perhaps other animal species are reservoirs for HEV. We aimed to study HEV seroprevalence in groups of people at risk for HEV infection as well as in pigs and wild boars in Estonia.

**Methods:** Totally 468 serum samples collected between 2007 and 2012 from 251 males and 217 females aged 17 to 63 years old were selected for the present study. From those, 205 samples were obtained from injection drug users (IDUs), 105 – from patients with chronic hepatitis C (CHC) and 158 – from veterinarians (VT). All serum samples have been tested for the presence of HEV IgG and HEV IgM antibodies using recomWell HEV IgG/IgM ELISA kits (Mikrogen, Denmark). For confirmation, anti-HEV IgG and IgM positive sera were tested with an immunoblot assay (recomLine HEV IgG/IgM, Mikrogen).

A total 380 serum samples from pigs below of 1.5 years of age collected from 14 Estonian swine farms and 471 meet-juice samples from wild boars collected across country were tested by PrioCHECK® HEV Ab porcine ELISA (Prionics AG, Switzerland) for detection of antibodies against HEV. RNA was detected by Real-time PCR using qScript™ One-Step Fast qRT-PCR Kit, ROXTM
Results: The overall anti-HEV IgG seroprevalence in studied people was 1.7%, being 2.4% (5/205) and 1.9% (3/158) among IDUs and VT, respectively. None one patients with CHC were found positive for HEV. We have also shown that 234/380 (62%) of serum samples collected from pigs and 89/471 (19%) of meet-juice samples were found positive for anti-HEV antibodies, indicating prior exposure to HEV. None of the tested serum samples from people and pigs were found positive for HEV RNA while the five meet-juice samples from wild boars were found RNA positive indicating the presence of acute/recent HEV infection.

Conclusions: based on serological data, HEV infection does occur in the adult Estonian population and is widespread among the Estonian domestic and wild animals. Thus, HEV can be a possible causative agent of acute nonA-nonC hepatitis in Estonia.
Hepatitis C virus prevalence in the Russian Federations: results of population study

Abstract No 26

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Categories

3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords

Hepatitis C, anti-HCV, age cohorts

Presentation type: Oral
Contact: karen-kyuregyan@yandex.ru
Submission date: 2014-03-22 21:14:11
Jury validation date: 0000-00-00 00:00:00

Abstract (english) (2550 characters)

Background/aim. Chronic hepatitis C is common viral infection in Russian Federation with its incidence 39.26 cases per 100,000 in 2013. Current hepatitis C virus (HCV) screening recommendations cover all patients with liver disease, blood donors, pregnant women and inpatients at the hospital admission. The aim of this study is to determine the proportion of HCV-exposed individuals who could be missed in current screening programs.

Methods. Anti-HCV (total) were tested using EIA in 3,703 healthy individuals with no previous HCV diagnosis in four geographically remote regions of Russian Federation – Sverdlovsk region, Khabarovsk region, Republic Tyva and Yakutia. About 900 individuals of
10 age groups (from < 1 year to > 60 years, about 90 individuals per group) were included in the study in each region. All anti-HCV positive samples were confirmed in EIA test for antibodies to structural and nonstructural antibodies to HCV.

Results. The average prevalence of anti-HC was 4.5% (41/910) in Republic Tyva, 3.9% (38/982) in Yakutia and 3.6% (31/871) in Sverdlovsk region. Surprisingly, very high anti-HCV prevalence (11.0%) was observed in Khabarovsk region. Different patterns of anti-HCV distribution in age groups were observed in each region. In Republic Tyva anti-HCV prevalence varied from 1.0% to 3.7% in individuals under 40 and peaked in age groups 40-49 (10,9%) and >60 (14,6 %). In Yakutia anti-HCV peak prevalence was observed in age groups 30-39 (9.6%, 13/136) and >60 (12.1%, 11/91), meanwhile in other age groups HCV prevalence was less than 5%. In Sverdlovsk region majority of anti-HCV cases was in children under 9 years (1-4 years – 5.9%; 5-9 years – 7.1%) and in adults of 30-39 years (6.1%), with only 3.0% anti-HCV positivity in individuals >60 years. In Khabarovsk region, most exposed to HCV age groups, based on anti-HCV detection, are 30-39 (22.5%), 40-49 (25,0%) and >60 (16.8%). Interestingly, in all four regions no positive for anti-HCV cases were detected in children under 1 year. Based on questionnaire data, all anti-HCV positive individuals are unaware of their status.

Conclusions. Our data demonstrate high rates of exposure to HCV in seniors and in individuals at middle age (30-49 years) who unaware of their infection status. Further population based studies are needed to confirm risk factors contributed to HCV spread in these cohorts and to determine the necessity of expanded HCV screening program in such age cohorts.
Kynurenine aminotransferase I and II activities in various types of brain pathology after HIV-1 Infection

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Categories
2. HBV, HCV, HIV: Pathology and Immunology

Keywords
kynurenine aminotransferase I and II, bronchopneumonia, brain pathology after HIV infection, D-cycloserine, kynurenic acid

Presentation type: Oral
Contact: halina.baran@neuro-lab.eu
Submission date: 2014-03-20 15:20:28

Abstract (english) (3047 characters)

Background and Aims: Kynurenic acid (KYNA), an intermediate metabolite of L-kynurenine (L-KYN), is a competitive antagonist of inotropic excitatory amino acid (EAA) receptors and a non-competitive antagonist of 7 alpha nicotine cholinergic receptors and its involvement in memory deficit and cognition impairment has been suggested. The biosynthetic machinery of KYNA e.g. the content of L-KYN and KYNA, and the activity of enzymes synthesizing KYNA, kynurenine aminotransferases I and II (KAT I and KAT II) in frontal cortex and cerebellum of HIV-1 infected patients in relation to different types of
Methods: Pathologies were classified as follows: HIV in brain (HIV); opportunistic infection (OPP); infarction of brain (INF); malignant lymphoma of brain (LY); and glial dystrophy (GD); and of control subjects. KAT I and KAT II activities were determined by enzymatic method. L-KYN and KYNA levels were determined by HPLC method.

Results: Within investigated pathologies the most frequent pathology was OPP (65%), followed by HIV (26%), LY, INF, and GD (each 22%, respectively). Further, 68% of HIV-1 patients had bronchopneumonia and the utmost incidence of bronchopneumonia was seen in the OPP and LY group by 60%. The KAT I activity increased significantly in the frontal cortex of all pathological subgroups, i.e. OPP = 433 % > INF > LY > HIV > GD = 182 % of CO, respectively. In the cerebellum, too, all pathological subgroups showed marked increase of KAT I activity (OPP = 326 % > LY, HIV > GD > INF = 181 % of CO). Whereas KAT II activity was only moderately increased in the frontal cortex of INF and OPP; in the cerebellum of HIV, OPP and LY was comparable to control, while mildly reduced in INF and GD. KYNA was increased significantly in the frontal cortex of LY (392 % of CO) and HIV (253 % of CO), and in the cerebellum of GD (291 % of CO; p<0.05). A significant increase of L-KYN was found only in the cerebellum of LY (333 % of CO; p<0.05). Interestingly, normal subjects with the diagnosis of bronchopneumonia were characterized by high KYNA metabolism in the brain, too.

Conclusions: The present study demonstrates a different pattern of alteration of KYNA metabolism in frontal cortex and cerebellum among investigated pathological subgroups of HIV-1 infected patients. A marked enhancement of KYNA metabolism in the brain has been found with occurrence of bronchopneumonia. This finding indicates a notable association between impaired conditions of oxygen availability and enhancement of KYNA formation in the human brain. These findings might have an impact on the understanding of pathological processes in the brain after HIV-1 infection involving the development of neuropsychiatric and neurological symptoms including memory and cognition impairment. Our recently published data on D-cycloserine about lowering KYNA synthesis strongly supports the significance of KYNA in the clinical manifestation of bronchopneumonia and AIDS encephalopathy. Corresponding author: E-mail: halina.baran@neuro-lab.eu
The study of environmental aerosols and indoor aerosols in classrooms for the presence of RNA of influenza A virus and DNA of *Mycobacterium sp.*

**Abstract no 28**

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**Categories**

4. Seasonal infections: influenza and tick born diseases

**Keywords**

Environmental research, Mycobacteria, Indoor aerosols, Molecular diagnostics, Influenza A virus

**Presentation type**: Oral  
**Contact**: t_grebennikova@mail.ru  
**Submission date**: 2014-03-20 16:16:01

**Abstract (english) (2805 characters)**

**Objectives:**
Monitoring of viral circulation in aerosols is very important for human health as of biosphere, and co-exist with human beings. Influenza A – contagious viral disease which causes seasonal epidemics, with different levels of mortality depending on the virulence of viral strains. Mycobacteria represented more than 80 different species. Most of these species cause mycobacterioses, but there are species that is also a danger to humans. It is important to monitor the presence of influenza in aerosols of the classroom, and environmental aerosols. In this paper the research about the detection of RNA influenza virus in aerosols of the classroom of the university during the seasonal epidemics 2011 y. and before its has been done. We also to detect of the DNA of Mycobacteria sp. in the indoor aerosols.

**Methods:**
Samples of environmental and indoor aerosols have been collected on the analytical aerosol filters AFA-RMP-3 with the device that allows for sampling on three filters simultaneously. There are 30 samples of the environmental aerosols and 20 samples of the indoors aerosols. The average rate of sampling was 16.0± 0.1 m3/hr. The time interval between the setting and removing the filters ranged from 4h to 8h. Filters have been used for RNA and DNA isolation.
and carrying out nested RT-PCR and subtyping and nested PCR.

**Results:**
The sensitive method for monitoring of viral RNA and bacterial DNA presence indoors and environmental aerosols has been developed. Samples of environmental aerosols been collected in places of birds gathering: rookery of Uria and Larus in small fiord of Kola Peninsula (Barents Sea), Anser anser in Yamal Peninsula, Anatinae in Skadar Lake. Influenza A Viral RNA in the environmental aerosols has been detected in 20% samples. DNA of the Mycobacteria sp. in the environmental aerosols has been detected in 25% samples. Indoor aerosols samples were collected and research in classrooms during lecture time. RNA of influenza virus during the epidemic 2011 year has been detected in 25% samples, then as after and before epidemic, RNA influenza A has not been detected. DNA of Mycobacteria sp. has been detected in the indoor aerosols samples in 25% samples.

**Conclusion:**
Influenza A Viral RNA has been found in the samples of environmental aerosols in places of birds gathering as well as in the samples of indoor aerosols during epidemic time. DNA of the Mycobacteria sp. has been found in environmental and indoor aerosols. The obtained data need to analyze and organize educational and preventive measures for the human in the future. Monitoring of the environmental and indoor aerosols can help for surveillance systems of epidemics, and provide hygiene recommendations and dissemination of knowledge in infectious diseases.
Alterations of L-tryptophan metabolism in the serum and cerebrospinal fluid in *Borrelia burgdorferi* infected patients

Abstract No 29

Berthold Kepplinger1,2,3,4*,5*, Brenda Sedlnitzky-Semler1,6, Carina Kronsteiner1, Jochen Reuss4, Nagy-Roland Badawi1, Roman Sobota5 and Halina Baran1,2,6*


* Former affiliation

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**Categories**

4. Seasonal infections: influenza and tick born diseases

**Keywords**

neuroborreliosis, kynurenic acid, tryptophan metabolite, kynurenine, serum, cerebrospinal fluid

**Presentation type**: Oral

**Contact**: berthold.kepplinger@neuro-lab.eu

**Submission date**: 2014-03-25 11:29:54

**Abstract (english)** (2889 characters)

**Background and Aims**: The tick-borne spirochaete, Borrelia burgdorferi, is the aethiological agent of Lyme borreliosis a disease, which mainly may affect the nervous system as well. Meningitis, cranial neuritis and radiculoneuritis are typical clinical manifestation during the acute phase and ongoing infection can cause chronic neurological manifestations. It is known that activation of tryptophan metabolism take place in various inflammatory diseases including neuroborreliosis. Patients with Borrelia burgdorferi infection were investigated by analysing the alteration of L-tryptophan (L-TRP) and L-TRP metabolite i.e. L-kynurenine (L-KYN), kynurenic acid (KYNA) and anthranilic acid (ANA) in the serum and cerebrospinal fluid (CSF).

**Methods**: Sample of serum and CSF from patients diagnosed with borreliosis (N=43; feminine/masculine ratio=20/23; range of age 63.8±1.5 years) and control subjects (N=8; feminine/masculine ratio=5/3; range of age 56.1±6.8 years) were collected from Neurological Department, Neuropsychiatric Hospital Mauer and from Neurological Department of the...
General Hospital Amstetten. For this investigation diagnosed patients were divided into subgroup as follows: definitive neuroborreliosis (NBO; N=34; feminine/masculine ratio=14/20; range of age 65.7±1.0 years) and probably neuroborreliosis (PNBO; N=9; feminine/masculine ratio= 6/3; range of age 56.3 ±5.6 years). TRP metabolites levels were determined by HPLC method. For significance ANOVA Test and Student’s t-test were used. Study performed according the Ethical Regulation of Low Austria.

**Results:** L-TRP level was significantly higher in the CSF (80 %; p<0.05) of NBO but not PNBO subgroup, comparing to control. The content of L-TRP in the serum of NBO and PNBO was mostly in control range. L-KYN levels were increased significantly in the CSF (800 %; p<0.001) and also in the serum (140 %; p<0.05) of NBO group, but not in the CSF and serum of PNBO, comparing to control. KYNA was increased significantly in the CSF (850 %; p<0.001) and serum (90 %; p<0.01) of NBO group, but not altered significantly in the PNBO, comparing to control. ANA content was increased in the CSF by 163 %, while in the serum of NBO and PNBO group a moderate increase was observed.

**Conclusions:** The present study revealed different alterations of L-TRP metabolism in the serum and CSF of patients infected with Borrelia burgdorferi. An enhancement of tryptophan metabolites L-TRP, L-KYN and KYNA was more pronounced in the CSF of NBO group than in the serum. An increase of ANA found in the CSF of NBO patients might be of importance for the later development of complex conditions seen in the infected brains. Study supported by NÖ Forschungs- und Bildungsges.m.b.H. (NFB) Project Nr. LS 10-032 Corresponding author: E-mail: halina.baran@neuro-lab.eu
The efficacy of DNA-immunization of mice is predetermined by the site of gene delivery and expression

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Categories
5. Vaccine Development

Keywords
intradermal, intramuscular, immune response, delivery, imaging

Presentation type : Oral
Contact : stefan.petkov@ki.se
Submission date : 2014-03-20 17:05:54

Abstract (english) (2516 characters)

The performance of DNA-immunogens depends on the efficacy of gene delivery and expression. Mechanistic studies are required to delineate the effects of delivery methods on the magnitude and specificity of the immune response they generate. We investigated the effect DNA delivery route on the strength of immune response against Th1- and Th2-type immunogens represented by protease (PR) and reverse transcriptase (RT) of HIV-1.

BALB/c mice were immunized with 20 µg of pVax-based humanized genes of PR, or multi-drug resistant RT intradermally/id or intramuscularly/im with subsequent electroporation. Plasmids were co-injected with a reporter gene encoding firefly luciferase (Luc). Gene delivery was monitored for 21 days by in vivo imaging of luminescence. On day 22, mice were sacrificed, spleens were removed, splenocytes were isolated and analyzed for their ability to produce cytokines in response to in vitro stimulation with peptides representing T-cell epitopes of PR and RT (IFN-γ/IL-2). Specific antibodies were determined by ELISA.

BALB/c mice received id and im injections of plasmids encoding HIV-1 PR, which induces a Th1- and RT, which induces a Th2-type of immune response. Intradermal expression of Luc+PR peaked on day 1, and intramuscular, on day 3 post-immunization. Expression of Luc+RT peaked 3 days post-immunization in both skin and muscles. For PR+Luc, bioluminescence dramatically decreased by day 15 in intramuscular, and by day 9 in intradermal immunizations. For RT+Luc mix, a significant loss of bioluminescence occurred on day 9 independently of immunization route; loss occurred at a higher speed than in the PR-recipients. The magnitude of T-cell response after immunization with Th1-inducing PR delivered id was 2-3 times higher than against PR delivered im. Id-delivery of the Th2-polarizing RT enhanced only the CTL-specific IL-2 response. Antigen-specific IFN-γ/IL-2
secretion correlated with the luminescence loss indicating that the expressing cells were cleared by a specific immune response. The use of bioluminescent reporters opens a new way to assess the input of delivery routes into the immunogenic performance of DNA-immunogens. Here we demonstrate that the outcome of DNA-immunization with the Th2-immunogen does not depend on the administration route, although the intradermal delivery contributes to an enhancement of cellular responses. On contrary, the performance of Th1-immunogens significantly benefits from the intradermal gene delivery.
Development of viral myocarditis transcriptomic biomarkers: selection of reference genes for normalization of qRT-PCR data in PBC and heart tissue

Abstract No 31

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Categories
1. Molecular Virology

Keywords
myocarditis, gene expression, reference gene, RT-qPCR

Presentation type: Oral
Contact: tsinakan@gmail.com
Submission date: 2014-03-20 17:16:22

Abstract (english) (2511 characters)

Viral infection has been recognized as the most common cause of myocarditis. In the endomyocardial biopsy (EMB) samples viral infection was found for enterovirus (32.6%), adenovirus (8.1%), parvovirus B19 (36.6%), and human herpesvirus 6 (10.5%). Myocardial inflammation followed by cardiomyocyte necrosis is always accompanied by changes in gene expression in affected cells, so transcription profiles may be considered as powerful biomarkers of viral myocarditis. Development of the viral infection in heart might alter gene expression not only in cardiomyocytes, but in the peripheral blood cells (PBC) as well. We analyzed expression of six housekeeping genes to select a set of reference genes for normalization of quantitative RT-PCR data to study transcription profiles specific for myocarditis.

PBC and EMB samples were obtained from patients and healthy donors, one orthotopic heart transplantation autopsy was used as healthy heart tissue. mRNA was isolated using in-house phenol extraction protocol and microcolumns, concentration was adjusted when possible.
Primers for qPCR were designed taking into account exon-intron structure of six commonly used candidate reference genes (GAPDH, ACTB, HPRT1, HMBS, RPL5 and B2M). Oligo(dT) primers were used for reverse transcription. qPCR was done using intercalating dye. Efficiency of amplification was determined using serial cDNA dilutions. Data analysis was performed using non-commercial software tools.

mRNA content of six candidate reference genes was analyzed in 27 samples: 16 samples from patients with viral myocarditis (7 PBC and 9 EMB) and 11 control samples (10 PBC and 1 autopsy). B2M, GAPDH, ACTB and RPL5 could be characterized as highly expressed genes, while HPRT1 and HMBS had low transcription levels. Limited amounts of mRNA isolated from EMB samples didn't allow to adjust mRNA concentration prior to RT-qPCR analysis, so routine algorithms of reference genes selection could not be applied in this case. Correlation was found between expression of ACTB and B2M genes in one group and GAPDH, HPRT1, HMBS and RPL5 in another.

Set of GAPDH and HPRT1 genes in our study was selected as a best choice for normalization of gene expression levels in myocarditis studies. Expression of GAPDH and HPRT1 genes is unaffected by myocarditis development and covers wide 25 – 35 Ct values range for RT-qPCR. Unification of reference gene set for heart tissue and PBC admit direct comparison of transcription profiles in clinical samples.
Development of the tools for PCR-detection of hepatitis A and C viruses in intrahospital viral contamination research

Abstract No 32

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Categories
3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords
Intrahospital Viral contamination

Presentation type: Oral
Contact: suzan_asper@yahoo.com
Submission date: 2014-03-20 18:25:12

Abstract (english) (2511 characters)

Objectives
The existence of viruses in healthcare settings represents a serious risk for both staff and patients. There were two tasks in the research: choosing the most sensitive PCR kit for detection of the hepatitis A and C viruses, as well as understanding how long time contamination with HAV and HCV is detectable on the surface.

Methods
PCR kits: “AmpliSence HAV-FL”, “AmpliSence HCV-Eph PCR” (Interlabservise, Russia) and laboratory developed primers for nested PCR was used for the research.
Viruses: Positive controls of viruses HAV (Cultured virus genotype A in inactivated bovine serum) and HCV (Serum from patients with chronic hepatitis C) was spread on surface. Samples were collected after 8, 24, 32, 48, and 56 hours.
**Results**

In order to select the most sensitive method, “AmpliSence HAV-FL” kit based on Real-time PCR, and nested PCR using laboratory developed primers were used for detection of HAV genome. It was found that Real-time PCR and nested PCR were able to detect 1 to 10 RNA copies of HAV. “AmpliSence HCV-Eph” kit and nested PCR using laboratory developed primers were used for HCV detection. Comparison of these analyses was shown, that nested PCR using home-made primers was more sensitive than PCR using “AmpliSence HCV-Eph” kit. So “AmpliSence HCV-Eph” detected $10^3$ RNA copies, while nested PCR could detect as low as 10 RNA copies/ml.

Then we tried to understand how long RNA of HAV and HCV could be detected on the surface after the contamination. Series of HAV dilutions were prepared from $10^5$ to $10^3$ RNA copies/ml. It was found that HAV in concentration $10^5$ RNA copies/ml remain detectable 56 hours after spreading on the surface; HAV in dilution $10^4$ RNA copies/ml was detected up-to 24 hours after, and HAV in dilution $10^3$ RNA copies/ml 12 hours after artificial surface contamination. A series of dilutions of HCV serum with known virus load was prepared containing from $10^7$ to $10^5$ RNA copies/ml. After surface contamination with a sample from sera containing $10^7$ copies/ml HCV RNA was detected up-to 32; $10^6$ RNA copies/ml, up-to 24 hours; and $10^5$ RNA copies/ml, up-to 8 hours post surface contamination.

**Conclusions**

HAV and HCV RNA is detectable on surfaces in laboratory environment from several hours to two days depending on the viral load in the contaminating sample. So they could be used for identification the level of intrahospital contamination. For HAV detection could be used both Real-time PCR and nested PCR, for HCV detection should be used nested PCR.
Design of DNA-immunogens based on the consensus protease of HIV-1 clade A strain predominant in the territory of the former Soviet Union

Abstract No 33

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Categories

5. Vaccine Development

Keywords

HIV-1 Protease, Consensus, Subtype A, Drug Resistance, DNA vaccine

Presentation type : Poster
Contact : Athina.Kilpelainen@stud.ki.se
Submission date : 2014-03-20 20:50:08
Jury validation date : 0000-00-00 00:00:00

Abstract (english) (2476 characters)

Russia suffers from a rapidly growing HIV epidemic. Highly active antiretroviral therapy (HAART) limits HIV-1 load and spread, but drug shortages and poor therapy compliance promote the emergence and spread of drug-resistant (DR) HIV strains limiting therapeutic options (Bobkova M, 2014).

Our goal is to design an immunotherapeutical which together with HAART would limit the development of drug-resistance, prolonging the effects of antiviral therapy. It is logical to base it on resistance-prone HIV enzymes. The aim of this study was to design its component targeting the protease (PR).

PR sequences from treatment-naïve patients infected with HIV-1 FSU-A were selected, aligned and a consensus FSU-A PR (PR_A) was created (MUSCLE). Primary mutations of resistance to PR inhibitors (PRI) and an inactivating mutation D25N were introduced into the PR_A gene by site-mutagenesis (Agilent Technologies). An epitopic map of PR variants was created using the IEDB analysis resource. A humanized gene for PR_A was synthesized and cloned for eu- and prokaryotic expression, the latter with a His-tag. PR_A was purified from BL21(DE3) E. coli cells using Ni-chromatography. PR expression was characterized by
Western blotting using anti-His-tag and anti-HXB2 PR antibodies (Fitzgerald). Protease activity of the protein and in cell lysates was assessed by FRET (Anaspec). The consensus PR of HIV-1 clade A strain FSU-A, and its inactive variant bearing D25N were designed. Expression of PR_A variants in HeLa cells and E coli was confirmed by Western blotting with polyclonal antibodies against HXB2 PR. D25N was shown to increase the expression and immunogenicity of clade B PR (Hallengärd D, 2011). Here as well, insertion of D25N led to a 5-fold increase of PR_A expression in E coli. PR_A was supplemented with mutations M46I, I54V, V82A conferring resistance to PRI in the clade A strains. DR-mutations were predicted to have no impact on MHC class I processing or MHC class II binding of PR_A-derived peptides. PR_A but not PR_A with D25N could cleave fluorescein-labeled peptide substrate. The activity tests for DR PR_A are on-going. PR_A genes will be incorporated into the consensus DNA-immunogens targeting drug-resistant HIV-1. High similarity of PR_A with PRs of other HIV-1 variants circulating in the FSU, namely CRF02_AG and CRF03_AB, indicates that PR_A based immunogens would be regionally adapted targeting the majority of local HIV-1 variants.
Standardization, validation and quality control are essential tools in the laboratory for safe conduct of clinical vaccine trials; experiences from Tanzania

**Abstract No 34**

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**Categories**

5. Vaccine Development

**Keywords**

vaccine trial, quality control, standardization, ELISpot, validation

**Presentation type**: Oral
**Contact**: charlotta.nilsson@folkhalsomyndigheten.se
**Submission date**: 2014-03-20 21:20:50

**Abstract (english)** (1732 characters)

Standardization, validation and quality control are essential tools for safe conduct of clinical vaccine trials; experiences from Tanzania

**Background**: For successful safe conduct of clinical vaccine trials standardized and quality controlled laboratory testing is essential.

**Methods**: In a phase I/II trial in Tanzania, laboratory procedures for the determination of the primary immunogenicity end point (IFN-γ ELISpot) were standardized, validated, and quality controlled to ensure accurate testing on site at the Muhimbili University of Health and Allied Sciences (MUHAS).

**Results**: Standard operating procedures (SOPs) for cell separation, cell counting, cryopreservation and ELISpot were established. Extensive training of the operators was conducted at the central study laboratory and on site at MUHAS. Operator proficiency was assessed in an operator validation test. Only those operators that accurately tested three samples with known responses at three time points, with a coefficient of variation <20%, were allowed to perform the assay. A total of 6 laboratory technologists successfully completed the operator validation. To determine the overall proficiency of the laboratory to perform the
ELISpot assay, the laboratory participated in proficiency testing. The MUHAS laboratory data was comparable with the results provided by the central study laboratory. Two phase I/II clinical HIV vaccine trials have successfully been completed by the MUHAS laboratory.

**Conclusion**: Extensive training and validation of operators and test procedures were important in order to determine the immunogenicity of a candidate HIV vaccine in Tanzania.
The HLA class II genotypes associated with sustained response to antiretroviral therapy (ART) in patients of AIDS

Abstract No P35

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Categories

2. HBV, HCV, HIV: Pathology and Immunology

Keywords

HLA, AIDS, Antiretroviral therapy

Presentation type: Poster
Contact: elenaeglite@inbox.lv
Submission date: 2014-03-21 10:10:56

Abstract (english) (3550 characters)

The HLA in humans controls immune response functions. One of the HIV hypotheses explains the greater inclination to the given pathology by the presence of particular HLA alleles, associated with the higher reactivity of immune system. Nowadays, one of the most important medical tasks is to find the most efficient and relatively safest treatment for HIV/AIDS. One of the ways to treat HIV/AIDS is Antiretroviral therapy (ART). However, in view of the HLA polymorphism it is necessary to determine the best association of ART with the HLA class II haplotypes. The purpose of the current study is to evaluate various HLA class II haplotypes with ART effectiveness in HIV-infected patients.

Materials and methods

The research included 350 HIV/AIDS infected patients. For monitoring there were used immunological parameters: amount of CD4+ lymphocytes and HIV viral load, which were observed in 24-48 weeks. The efficacy criteria of ART: HIV RNA viral load <400 cop/ml - after 16-24 weeks. Increase of CD4+ cell amount of 30-70 cells/µl after first 3 months and of 100-150 cells/µl after a year. Absence of new opportunistic infections after three months of ART treatment. Genomic DNA was isolated from PBMC by using the QIAamp DNA blood kit (Qiagen). HLA class II alleles DRB1, DQA1, DQB1 genotyping was performed using RT-PCR method. Results: Before treatment CD4+ cell count amount median in all patients was 155 cell/µl and HIV RNA viral load median - 55000 cop/ml. By studying the HLA class II haplotypes, it was concluded that the highest association with high immunological efficacy has haplotypes HLA-DRB1/DQB1/DQA1 01:01/06:02-8/01:03, 01:01/03:01/03:02, 01:01/03:02/01:03.
After 12 weeks of treatment, CD4 + lymphocytes amount in the particular group has increased to 600-700 cell/µl, HIV RNA viral load has decreased to 5 000 cop/ml. After 24-48 weeks of treatment - CD4 + lymphocytes amount has increased to 806-900 cells/µl (450 - 500 cells/µl), and HIV RNA viral load has decreased <400 copies/µl (decrease by 20 - 30 000 cop/µl). These data suggest an efficiency of ART, as none of the patients in study groups with existing haplotypes has showed HIV clinical progression (the development of opportunistic infections) during the treatment. At the same time the association of low immunological efficacy has haplotypes: HLA-DRB1/DQB1/DQA1 15:01/03:01/03:01, 17:01/05:01/02:01, 17:01/03:01/05:01, 07:01/03:01/02:01, 11:01/03:01/05:01, 15:01/03:02/01:02, frequency (gf = 0.03/0.04/0.05). Patients with particular haplotype, treatment contribute to progressive CD4 + cells amount increase in the blood, and reduce the HIV viral RNA load in the study group of HIV/AIDS patients. After 12 weeks of treatment a tendency to increase in CD4 + cell amount was formed, but the increase was not large (50-100 cells/µl), HIV RNA amount decreased an average of 2000 cop/ml. Sufficiently high rates of HIV RNA were maintained after 24 - 48 weeks of treatment (55 thousand copies/µl). In study groups with this specific haplotypes 12 weeks after the start of ART latent opportunistic infections flare and side effects (diarrhea, vomiting, etc.) were observed. **Conclusions** The given data shows efficiency of ART therapy. No clinical progression of HIV (worsening of latent opportunistic infections) was observed during the ART treatment in study groups with existing haplotypes.
The HLA class II molecules play a central role in regulating the immune response of HIV-infected patients in AIDS stage

Abstract No 36

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Categories

2. HBV, HCV, HIV: Pathology and Immunology

Keywords

HIV, HLA class II, exon 2

Presentation type: Poster

Contact: diana.kasjko@gmail.com

Submission date: 2014-03-21 10:22:32

Abstract (english) (2665 characters)

Since the HLA class II molecules play a central role in regulating the immune response, they may have an important role in controlling resistance and susceptibility to the infectious diseases. The AIDS stage of HIV infection is associated with impaired immunity. The level of response is determined by genetic factor that interacts to determine the outcome of the disease. HLA class II provides the strongest genetic contributions to infection diseases and inflammatory disorders. However, the mechanism by which particular HLA alleles confer disease risk and protection has not been fully explained by known structural and functional variations in HLA proteins. **Aims:** To find out whether ongoing missense mutations in the exon 2 of DRB1*01:01 affect the operation of this protective allele in HIV patients.

**Methodology:** This is the pilot study of HLA DRB1*01:01 exon 2 in a sub-population of Latvia. The study includes 100 AIDS stage of HIV-infected patients from Riga Eastern Clinical University Hospital, “Infectology Center of Latvia”. The biological material used for the study is stored in the Clinical Immunology and Immunogenetics Laboratory of Riga Stradiņš University. All of the patients chosen for this study are in the AIDS stage of HIV infection. DNA was isolated from venous blood samples using the Qiagen QIAamp DNA kit reagents and the exon 2 nucleotide sequence of HLA was determined by the automatic sequencing – “Big Dye Terminator mix” (Applied Biosystems, USA). Statistical analysis was performed using Microsoft Excel, DOS StatCalc programs. The significance of the differences in indicators was evaluated according to reliability p£0.05. The odds ratio was
calculated according to Wolf’s method. **Results:** We found missense: at codon 47 – in 80% of cases; at codon 67 – in 20% of cases; at codon 75 – in 11% of cases; at codon 82 – in 10% of cases; at codon 86 – in 10% of cases (p<0.05) (See Table 3). One of the HIV patients had a STOP-codon (codon 13). Besides, a balance between nucleotide transversion and transition has been observed, suggesting mutations in the exon 2 (transversion in a human genome is rare)(OR 0.05, 95% CI 0.00-0.053). **Conclusion:** The results of the study are not complete in order to be able to say conclusively that the existing mutations in the exon 2 of HLA-DRB1 *01:01 gene cause wrong immune response, thus the protective functions of this allele are not fulfilled. For a fuller understanding of the importance of ongoing mutations in the exon 2 in the development of HIV/AIDS, it is necessary to increase the study group.
Trends in HIV testing coverage among target groups in Lithuania, 2009-2013

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Categories
3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords
HIV, testing, risk groups

Presentation type : Poster
Contact : irma@ulac.lt
Submission date : 2014-03-25 07:37:42

Abstract (english) (1667 characters)

Background: High risk groups and especially their sexual partners (bridging populations) are at the highest risk of HIV transmission. STI patients, IDUs, MSM, SW and other groups in Lithuania are the target groups, whom HIV testing is recommended by the Order of MoH. Some changes in HIV testing among target groups were observed in the last five years.

Methods: Retrospective analysis of National HIV testing databases of the Centre for Communicable Diseases and AIDS was performed. Objective was to assess trends in HIV testing coverage among target groups in Lithuania from 2009 up to 2013.

Results: In total more than 900,000 people were tested for HIV in Lithuania from 2009 up to 2013. General HIV testing coverage increased during observation period: from 190,530 tested people in 2009 to 221,293 in 2013. In the last five years HIV testing increased threefold in persons who voluntarily applied for testing and twofold in persons tested for clinical indications. In 2013 HIV testing among target groups increased as compared to 2009 respectively: 50.6% in IDUs, thirteenfold in MSM, threefold in CSW, ninefold in the group of persons who had more than one sexual partner and twofold in the group of persons who had sexual contact with HIV positive person. HIV testing among STI patients was increasing from 2009 up to 2010 and in 2013 62.6% decrease as compared to 2010 was observed.

Conclusions: Increasing coverage of HIV testing in general population and among target groups shows growing consciousness of residents and improved access to HIV testing for
target groups. Despite this, a lack in HIV testing among STI patient is still a concern.
The role of media in the modern world of life science

Abstract No 38

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Categories
9. Viral infections and alcohol and drug dependence

Keywords
consulting, media, networking, business, Internet

Presentation type: Oral
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Submission date: 2014-03-24 10:48:20

Abstract (english) (2549 characters)

Bio-Tech Media is leader of media dedicated to life science area. Company is a publisher of websites: Biotechnologia.pl, CEBiotech.com, Laborant.pl and two quarterly magazines. From beginning of its foundation Bio-Tech Media is focused on supporting Central European bio-sector on different levels. Company constantly updates its websites with the freshest news from life science area, including science, business, industry and economy issues; facilitates creation of business networks thanks to internet platform which gathers representatives branches such a Biopharmacy, Biotechnology, Cosmetology, Universities, CRO companies, raw materials producers and suppliers etc.; organises workshops and trainings in some of mentioned areas. Bio-Tech Media does not have any external funding and its business model is unique in the European scale.

Tools

-Biotechnologia.pl is leading polish website dedicated to widely understood area of biotechnology, biopharma, cosmetology, and innovative bio-business. The first and the richest source of specialist bioindustry information and full business offer for life science enterprises.

-Laborant.pl: new brand portal dedicated to widely understood laboratory industry. Independent tests of laboratory devices and equipment, database of laboratory calculators, news, articles etc.

-CEBiotech.com is the 1st Central European Networking Platform integrating laboratories, institutions, contract researchers, consulting and other businesses from Central and Eastern Europe. Website represents the wide range of laboratories, institutions, contract researchers, consulting and other businesses from the Life Science sector in Central European Region.
- Biotechnologia.pl the quaterly magazine - new position in portfolio of Bio-Tech Media which contains exclusive interviews, articles and elaborations prepared by editors of the Biotechnologia.pl website.

- Laborant the quaterly magazine - each edition is focused on different subject in life science area.

All the Bio-Tech Media's websites generate more than 500,000 visits per month. The newspapers have a circulation of 5,000 copies each. Together they are a great tool to promote Central European bio-sector in the region and internationally and also they are a platform where people have an opportunity to exchange their experience and knowledge. Bio-Tech Media's tools could be an effective method to describe and present various research and constitute the best way to disseminate of scientific results in a manner understandable to all.
Incidence of acute hepatitis E in the Russian Federation

Abstract (english) (2741 characters)

Background/aim. Viral hepatitis E (hepE) is infection caused by hepatitis E virus (HEV), which has broad but uneven distribution. According to WHO, the disease is most common hepatitis in the world. High mortality rates among pregnant women and the presence of large outbreaks determine attention to this infection. Initially it was thought that hepE is widespread only in developing countries in tropical areas. It was believed earlier, that cases of hepE in developed countries were sporadic and related to the importation of high endemic regions. Increased incidence of hepE is currently registered in countries such as Britain, France, Germany, the U.S. and others. The number of non-imported, autochthonous cases of hepE is also increased in Russia. 2013 was the first year of official registration of hepE in Russia. The aim of this study - to perform the analysis of hepE incidence rates in different regions of Russian Federation and to analyze the long-term dynamics of hepE incidence in the Belgorod region, the endemic region for hepE.

Methods. Data on infectious and parasitic diseases incidence (acute hepatitis E, Form 1) for January - December 2013 provided by the Federal Service for Supervision of Consumer Rights Protection and Human Well-being were analyzed for each region of Russia. To assess the dynamics of morbidity (2010-2013) for hepatitis A and hepatitis E data from Federal
Service for Supervision of Consumer Rights Protection and Human Welfare in the Belgorod region were used. Social and epidemiological analysis of hepE cases was based on data presented in the emergency notification and medical history of patients in the Belgorod region. Results. Total 92 hepE cases were notified in 2013 with incidence 0.06 per 100,000. All cases were detected in adults. Analysis of HEV associated morbidity by Federal Districts demonstrated the presence of reported cases of infection in 5 of the 7 districts. The largest index was registered in the Central Federal District - 0.18 per 100,000 (70 cases). HepE cases were reported in 23 of 86 territorial units (27%) of Russia with fluctuating rate from 2.15 per 100,000 (33 cases, Belgorod region.) to 0.02 per 100,000 (Trans-Baikal region). In 2011-2013 years more than 100 cases of acute hepE were reported in Belgorod region. During that time the proportion of hepE in total numbers of acute hepatitis cases in Belgorod region was 54.4%. These figures are the highest in the Russian Federation. The most common acute hepatitis infection in Russia is hepA, but in Belgorod region in 2011 - 2013 the incidence of acute hepE exceeded incidence of hepA. Conclusion. The results obtained indicate HEV circulation and its implications for health care in Russia.
Different phylogenetic models applied for transmission of HCV among IVDUS in Malmö

Abstract No 40

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Categories
3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords
Hepatitis C virus, intravenous drug abuse, transmission, molecular epidemiology, phylodynamics, phylogeography

Presentation type : Oral
Contact : anders.widell@med.lu.se
Submission date : 2014-03-18 15:38:49

Abstract (english) (3045 characters)

Background: The major source of HCV infections in industrialized countries is the intravenous drug addicts (IVDU) population. In Sweden, we have earlier presented data from a needle exchange program on the incidence and viral dynamics around HCV seroconversion. Aims: Comparisons between different phylogenetic models which can include large numbers of sequences

Methods: Two different phylogenetic models in Mega 6, the neighbor-joining (NJ) and maximum likelihood (ML) algorithms, respectively, were compared using the same nucleotide substitution method (Tamura –Nei), the same Gamma and other settings, including 400 bootstrap (BS) replications. In all, 413 IVDU partial (319 ntc) NS5B sequences from the Malmö 1997 and were tested together with 125 corresponding GenBank sequences, representing genotypes 1-7 and several subtypes. Trees were evaluated both at the widely accepted > 70% BS level and also tentatively widened to > 60-69% BS level.
Results and discussion: When aligned, the included dataset had a transition/transversion rate of 4.7/1 with many differences within subtypes at third base positions. Trees were shallow within each subtype, in contrast to the differences between subtypes or more so, between genotypes. The diversity information in the investigated segment was moderate, which may reflect functional constraints of the phenotype(s) within each subtype/genotype. The large genotype 1a tree, showed 20 BS>70% clusters by ML and 18 by NJ; two discordant sequences at cutoff with 70%, 70% by ML, respectively, dropped to 69% and 65% by NJ, respectively. In contrast, one cluster with BS70% by NJ was BS65% by ML. Otherwise clustering was concordant. Clusters contained two to nine sequences, mostly two to three. Three additional clusters appeared with BS60-69%. The small subtype 1b tree at >BS70% contained only two small, concordant clusters. At BS60-69% one 15 member cluster was added with BS63% by ML only. As for subtype 2b, six concordant clusters were seen, one broadening at the BS>60% level by ML. The large genotype 3a sequence set, contained 15 ML/NJ concordant clusters with BS>70%, mostly with only two to three members each. One sample with ML BS78% in the root of a cluster became unlinked within the 3a samples by NJ. One cluster with BS71% by ML turned it into two groups by NJ. At BS60% for this subtype gave two additional clusters by ML, which however fell below 60% by NJ.

Conclusion: The two different models ML and NJ produced highly concordant identification of significant clusters. The minor discordances were linked to that BS for clusters in general were stronger in the ML model. Within genotypes, the trees were flat and clusters, 45 in all, generally narrow with few members each. Many contained both incident HCV infections as well as chronic. Our method comparison is one step in a planned study of HCV phylodynamics and phylogeography in the Baltic Sea region countries, both for choice of target region and phylogenetic model where other models will also be evaluated e.g. PhyML.
Influenza, pandemix vaccination and narcolepsy: review of some recently published laboratory findings

Abstract No 41

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Categories
5. Vaccine Development

Keywords
Narcolepsy, Vaccination, Pandemrix, Side effect, T-cell mimicry

Presentation type: Oral
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Submission date: 2014-03-21 15:36:18

Abstract (english) (3553 characters)

Background. The Spanish Flu H1N1 swept the world in 1918-1919 as a devastating pandemic, killing more than 40 millions. In 2009, reports from Mexico of a new rapidly spreading influenza porcine like H1N1 variant with serious clinical course. Since this “swine flu” became a pandemic, WHO experts urged the manufacture and use of a vaccine against the circulating strain H1N12009pdm. Vaccines were manufactured by major producers based on well known procedures. To increase immunogenicity, some producers used adjuvants and the Pandemrix vaccine had squalene. Despite a mild pandemic, a serious side effect surfaced in Scandinavia months after the vaccination ended – narcolepsy, a disabling sleep disorder, often linked with cataplexy. This side effect affect several hundreds, mainly children and adolescents who now face life long disability. Narcolepsy has no known etiology, but is linked with the loss of hypothalamic neurons producing the neuropeptide hypocretin (HCRT). In China, where H1N12009pdm vaccination was not used, an increased incidence of narcolepsy occurred months after the peak of the pandemic.

Recently study. 98% of all narcolepsy cases share the HLA–DQ haplotype, DQA1*01:02/DQB1*06:02, and express the DQ0602 heterodimer on antigen presenting cells. DQ0602 seems necessary for narcolepsy development but is present in 20-30% of humans, the vast majority never getting narcolepsy. The Stanford group, has now investigated T-cell mimicry and binding of the MHC II DQ0602 to patient CD4 cells in presence of different peptides (De la Herrán-Aritaet et al, Science Translational Medicine, Dec 2013). Using overlapping peptides covering HCRT and their potential of binding to DQ0602 and subsequently to CD4 cells, and measuring γ interferon in an ELISpot assay, two unique short, similar peptides (HCRT53-67, HCRT85-99) were found. Both peptides by ELISpot discriminated between controls (few foci) and narcolepsy (many foci), indicating that narcolepsy patients had CD4
cells which recognized HCRTs when presented on DQ0602. Findings were corroborated in homozygous twins, where one had narcolepsy and the other not, and in Pandemrix vaccinated children where one got narcolepsy and the sibling did not. Subsequently the team identified key binding amino acids of the HCRT both to the MHC anchor/groove and to the T-cell receptor recognition on the CD4 cell.

They proceeded to vaccinate narcolepsy patients and controls with a non-adjuvated, trivalent vaccine containing H1N12009pdm, and found numbers of ELISpot foci against HCRT to increase in narcolepsy patients – in the same range as influenza – but the picture was stronger in vitro using vaccine the trivalent vaccine. Subsequently H1N12009pdm proteins were scanned for DQ0602 binding peptides. One hemagglutinin peptide, pHA1275-287, sharing some key amino acids with the HCRTs, was, if preincubated with cells, enhancing a following stimulation of HCRT53-67, HCRT85-99 in a cross-reactive way, stronger so if patient CD4 cells were enriched.

The authors conclude that their studies have shed new light in the relation between DQ0602, hypocretin and Pandemrix peptides, but sequential events leading to narcolepsy remain unknown. They also found HCRT reactive CD4 cells in a stored patient sample, from 1998, indicating CD4 stimulation before Pandemrix. Another caveat was that it was that human neurons themselves do not express MHC II. Nevertheless this is definitely a new approach indicating T-cell mimicry.
The new round 2014-2020 for European Union funding instruments - opportunities to all

Abstract No 42

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Categories
9. Viral infections and alcohol and drug dependence

Keywords
Infectious diseases, Horizon2020, ERA-NET, HIVERA, INFECT-ERA

Presentation type: Oral
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Submission date: 2014-03-23 11:58:47

Abstract (english) (2745 characters)

The first Workprogrammes of the new Research and Innovation Framework Programme Horizon 2020 http://ec.europa.eu/programmes/horizon2020/ while following the established structural form like FP6 and FP7, nevertheless, has introduced some novelty. For instance, the Societal Challenge 1 – Health, demographic change and wellbeing – in the first WP for years 2016 – 2017 puts a very broad topic „PHC 1 – 2014: Understanding health, ageing and disease: determinants, risk factors and pathways” as the first topic in the biomedicine related „personalized Healthcare” – PHC – part. Since the call for stage 1 for this topic just closed, it will be interesting to see how many proposals were submitted to this call.

Asides of the broad „bottom-up” topics, some focused initiative have found their place in the Workprogramme. On the part of infectious diseases they are vaccine development topics against TBC and HIV/AIDS. The financial power of respectively 15-25 and 15-20 million EUR makes substantial impact possible. At the moment it is open, if further Workprogrammes 2016-2017, 2018-2019 and 2020 could contain focused topics on the part of infectious diseases.

The rules for participation have improved in the sense that 100% funding from EU is possible for Research and innovation actions and for selected Innovation actions if shown in the Workprogramme. On the other hand, access to the H2020 from outside of EU has become stricter. For instance, Switzerland and Russia are not anymore automatically eligible for funding from Horizon2020. They will cover their costs themselves. This can, however, improve as the programme evolves. Happily, all Eastern partnership countries are eligible for funding from H2020.

H2020 will be richer in supporting European Research Area (ERA) instruments. There will be a dedicated co-fund scheme for ERA-NETs. All ERA-NETs under H2020 will be
combination of the former ERA+ and ERA-NET under FP6/7. In the area of infectious diseases the well known INFECT-ERA (former PathoGenoMics) http://www.infect-era.eu joins 11 countries, has an active joint call programme, two more calls are planned in 2015 and 2016. A new co-funded ERA-NET is planned to start in 2017. The ERA-NET HIVERA with 9 country participation is devoted to ERA in HIV/AIDS research. One more call is in discussion for 2015, and in 2016 a new co-funded call is planned.

The Article 185 initiative EDCTP will transform into continuation initiative EDCTP-2 encompassing the traditional TBC, malaria, HIV/AIDS research, but also adding research on neglected tropical, in particular parasitic diseases. The negotiations on consortia composition are in discussion.
Vertical transmission of HIV infection in twins

Abstract

Background and Aims In Latvia the first case of HIV transmission was registered in 1998. On January the 1st, 2014, number of HIV infected children aged 1m.-16y.o. was 59. Advanced HIV disease in mother associated with likelihood of transmission to infant. It is known that twins born first are at higher risk of HIV infection. Aim of study was to analyze the cases of twins born to HIV-1 infected mothers enrolled in care in Latvian Center of Infectious disease (2007-2013).

Material and Methods. We investigated 9 twin pairs, who were born in 2007-2013 (in...
2007-1, 2010-1, 2012-2, 2013-5). Through Caesarean section delivered 7 twins, vaginally – 2, sex identical were 6 pairs (boys - 2, girls – 4). For diagnoses of HIV infection in infants ELISA kits for the detection and confirmation of HIVp24 core Ag (Innotest) and rt-RT PCR kit (Cobas AmpliPrep/TaqMan HIV-1 system, Roche) for HIV RNA detection (detection limit 20 cop/ml) and quantification were used. CD4 + cell count were detected by flow cytometry. Third generation MEIA assay (ABBOTT) was used for the demonstration of anti-HIV seroreversion in uninfected infants.

Results: The first twin pair was presented to hospital in 2007, then 1 and 2 in 2010 and 2012 accordingly. Significant increasing of twins (5) born to HIV-1 infected mothers was observed in 2013. Prematurity (31-37 weeks) of deliveries observed in 89% (8/9) and maternal age >30 (56% - 5/9) were regarded as a risk factors. Mother’s viral load was from undetectable (2/9 – 22%) to 10^5 cop/ml (1/9 – 11%), more often (6/9 - 67%) from 10^2 (min- 5.9 x10^2) to 10^4 (max- 7.7 x10^4), CD4+ - from 174 to 816 cells /mm^3, only in 1 (11%) > 700, as an additional risk factor - in 3(3/9 – 33%) < 500 cells/mm^3 (174-396). Five HIV-1 infected mothers received antiretroviral therapy (2 – from 14 weeks of pregnancy, others – from 23, 25 and 30 week), four didn’t. At time of first visit (as a rule at age 5 - 9 weeks, 1 twin – at 10 month) all 18 infants have negative HIV-1 Ag and 16/18 (89%) - undetectable level of HIV viral load. Two first born children from different twins have detectable HIV-1 viral load - 7.2 x10^2(Caesarean section) and 1.2x10^5 cop/ml (vaginally delivery), one was born to mother who didn’t receive antiretroviral therapy, the other – to mother who began ART at week 25 of gestation. The rest infants hadn’t detectable HIV RNA and HIV antibody in age 14-24 m. or till now are on follow up with no detectable HIV RNA and seroreversion trend in levels of HIV antibodies.

Conclusion: Number of twin deliveries from HIV-1 infected mothers increased in Latvia, like in other industrial countries. Recently vertical HIV transmission is proved in 2/18 infants from twin pairs, both first born to mothers, which didn’t receive antiretroviral therapy. Most twin’s mothers have one or more vertical transmission risk factors (age, born prematurity, viral load, CD4+ count).
Acute viral hepatitis C: treatment with pegylated interferons

Abstract No 44

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Categories

Keywords
acute viral hepatitis C, Pegasys, Copegus, markers, ARN-VHC

Presentation type: Poster
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Submission date: 2014-03-23 15:24:02

Abstract (english) (2640 characters)

Statement of purpose. To determine the efficiency of the antiviral treatment combined by Pegasys and Copegus in acute viral hepatitis C.

Methods used. 40 patients were included in the study with acute hepatitis C. To confirm the diagnosis, anamnesis data were analysed, as well as clinical, epidemiological and laboratory ones. We investigated: the hemoleucogram, liver biochemical tests (bilirubin, ALT, thymol test, prothrombin) the markers of viral C hepatitis (anti-VHC IgM, anti-VHC tot) excluding other viral hepatitis (by determining of the viral B and D hepatitis markers), the abdominal echography and ARN-VHC by PCR. A combined antiviral treatment was started with Pegasys+Copegus.

The results. Clinical symptomatology was characterized by a general fatigue in 100,0% of the patients, nausea in 50,0%, vomiting – 25,0%, loss of appetite – 60%, pains in the left hypocondrium and epigastrium – 70,0%, fever – 25,0%, arthralgias – 40,0%, juandice – 70,0%, hepatomegaly – 100,0% and splenomegaly in 40,0% of the patients. The epidemiological anamnesis established that in 60,0% of the patients, infecting was due to parenteral interventions, sexual relations – 10,0%, blood donors – 5,0%, by habitual way – 10,0%, while in 10,0% of the patients, there were not determined the days of infection. An acute onset of the disease was registered in 40,0% and a slow one in 60,0%.

Hyperbilirubinemia consisted 126,5±18,2 mmol/l, ALT – 11,09±0,5 mmol/l, thymol test 3,8Un, the prothrombin index 84,3±2,1%. Anti VHC IgM and anti-VHC tot were revealed in all 40 patients while ARN-VHC varied from 800.000 copii/ml to 3,8 mln copii/ml. The length of hospitalization consisted on an average 14,05±1,28 days. Pegasys was administred 180 microgramms s/c once a week for 3 months in 16 patients, 6 months in 16 and 12 months – in 8 patients plus Copegus 1000-1200 mg a day in addition. After 3 months of treatment ARN-VHC was not found in any of the patients. The decision to continue the treatment up to 6 and 12 months was taken with increased values of ALT. The patients who underwent a tretment...
for 6 and 12 months no ARN-VHC was revealed and ALT became normal. In 6 an 12 months after treatment the ARN-VHC was negative in all the patients.

**Conclusions:** The parenteral infection being a prevalent way in 60,0% and the sexual 10,0%. The acute onset of the disease was registered in 40,0% and the slow one in 60,0%. The virological sustained response of the combined treatment Pegasys+Copegus in acute viral hepatitis C was 100,0%.
Complexity and diversity of hepatitis B virus quasispecies during long-term antiviral therapy

Abstract No P45

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Categories
1. Molecular Virology

Keywords
HBV, lamivudine treatment, quasispecies, preS deletion.

Presentation type : Poster
Contact : jansons@biomed.lu.lv
Submission date : 2014-03-24 07:23:01

Abstract (english) (2311 characters)

BACKGROUND. Hepatitis B virus (HBV), because of its error-prone viral polymerase, has a high mutation rate leading to widespread substitutions, deletions, and insertions in the HBV genome. Deletions may significantly change viral biological features complicating the progression of liver diseases. However, the clinical conditions correlating to the accumulation of deleted mutants remain unclear.

METHODS We explored HBV deletion patterns and their association with disease status and antiviral treatment by performing amplification of Pres1/Pres2/S/P region of HBV genome,
cloning of obtained amplicons and sequencing of clones. Two chronic hepatitis B patients infected by D genotype virus developed resistance to lamivudine treatment were selected for the study. The serum samples were regularly collected during 5 years.

RESULTS. In both cases emergence of antiviral drugs resistant mutations in YMDD domain of polymerase gene of HBV was not discovered during all period of observation. But on the other hand, in both cases we found deletion variants of preS region existing as a *quasispecies*. We found that some of them was persisted in the population during more than 5 years of observation without significant changes. In a case of first patient preS1 deletion variants were often associated with STOP mutation in preS2 region that prevents expression of L and M surface proteins.

CONCLUSIONS. The phenomena of PreS deletion variants of HBV accumulation during antiviral treatment was described in many scientific publications, but in our study we seen not just arise of mutated forms but wavelike dynamic changes in *quasispecies* population of virus. It is noticeable that in both cases increasing of deletion variants proportion in the population of *quasispecies* was associated with exacerbation of HBV infection. The deletions in PreS region alone cannot be cause of lamivudine resistance of HBV, but they may promote HBV immune escape after recovery of host immune function following antiviral treatment. The successful replication of L and M surface proteins defective forms of HBV may be explained by coexisting of HBV *quasispecies* not only in whole host organism but also in single infected cells, in that case minor fraction of normal viral genomes can work as a helper for the deletion variants.
Prevalence of hepatitis A, B and C serological markers among first-time remunerated blood donors in Lithuania: interim results

Abstract No P46

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Categories

3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords

Hepatitis B, Hepatitis C, Serological markers, Prevalence, Blood donors

Presentation type: Poster
Contact: arvydas.ambrozaitis@elnet.lt
Submission date: 2014-03-23 20:32:14

Abstract (english) (1134 characters)

Statement of purpose. The aim of this cross-sectional study was to estimate the prevalence of hepatitis A, B and C serologic and virologic markers among the first-time non-remunerated blood donors in Lithuania.

Until now, viral hepatitis remains an important public health problem worldwide, in the European Union, and in Lithuania. The last study of population serological markers of viral hepatitis prevalence in Lithuania was conducted more than 8-10 years ago. The primary objective of this study was to evaluate the prevalence of anti-HAV, HBsAg, HBV-NAT, anti-HBc, anti-HBs, anti-HCV and HCV-NAT among the first-time non-remunerated blood donors from the National Blood Center in Vilnius in 2011-2013. Total of 250 adult first-time non-remunerated blood donors were included into the study; 111 males and 139 females.

Results. Total of 36 (14.4%) were positive for anti-HAV, 1 (0.4%) - for HBsAg, 1 (0.4%) - for HBV-NAT, 5 (2.0%) – for anti-HBc, 129 (51.6%) - for anti-HBs, 5 (2.0%) - for anti-HCV, 4 (1.6%) – for HCV-NAT. All 200 sera samples tested for anti-HEV were negative. The study is in progress.
Prevention of influenza-virus induced pulmonary histopathology in mice using antivirals and antisense oligonucleotides to inducible nitric oxide synthase

Abstract No 47

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Categories

4. Seasonal infections: influenza and tick born diseases

Keywords

Influenza virus, Pneumonia, Nitric oxide, antisense oligonucleotides, Zanamivir

Presentation type: Poster
Contact: arvydas.ambrozaitis@elnet.lt
Submission date: 2014-03-23 20:48:13

Abstract (english) (2297 characters)

Statement of purpose. The studies on influenza virus infection in mouse model demonstrate that overproduction of free radicals, including nitric oxide (NO), is implicated in the development of pneumonia. High-output levels of NO are produced by activating the inducible nitric oxide synthase (iNOS) in macrophages. It is known that suppression of the iNOS activity with its inhibitors reduces the pulmonary pathology in mice during influenza virus infection. However, there are no evidences provided in the literature that the influenza virus-induced pulmonary histopathology in mice can be prevented using antivirals combined with antisense oligonucleotides targeting iNOS expression.

Materials and methods. The BALB/c mice were challenged with A/PR/8/34 (H1N1) influenza virus and treated intranasally with saline (placebo), neuraminidase inhibitor – zanamivir (2 mg/kg), antisense oligonucleotide (100 μg) to iNOS mRNA or their combination daily. After 5 days of the treatment, the mice were euthanized and their lungs were excised, formalin-fixed, paraffin-embedded, hematoxylin and eosin-stained. The samples were analyzed microscopically in a blinded approach using the coded slides. The degree of perivascular
lymphocytic, peribronchial lymphocytic and focal leucocytic infiltrations, bronchiolitis, hemorrhagia, hyperemia, damage of epithelial cells, alveolar macrophages, diffuse leucocytic infiltration, capillary thromboses, pleuritis, alveolar collapse, fibrosis, hyaline membranes and edema were independently scored on an increasing scale from 0 to 3. The mean of sum of histological scores was compared between the experimental mice groups. Statistical analyses were performed with SPSS 21.0 package program.

Results. Statistically significant differences were found between the histological changes of influenza virus-infected and treated with zanamivir and/or antisense oligonucleotide to iNOS, compared to placebo treated mice (p<0.05). There were no differences of histological changes between zanamivir or antisense iNOS oligonucleotide treated mice groups.

Conclusions. The treatment with neuraminidase inhibitors and antisense iNOS oligonucleotides reduces the lung damage caused by free radicals produced in response to influenza virus infection in mice.
Trends in unknown modes of HIV transmission in Lithuania, 2009-2013

Abstract No 48

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Categories

3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords

HIV, transmission, unknown mode

Presentation type : Poster
Contact : irma@ulac.lt
Submission date : 2014-03-25 07:40:45

Abstract (english) (2005 characters)

Background: in the last five years (2009-2013) a number of health care institutions that conduct HIV testing increased by more than 15%. HIV incidence increased slightly from 5.4 in 2009 to 5.98 cases/100000 population in 2013. According to the Order of MoH, accumulation of epidemiological (including behavioural) data on new reported HIV cases is a part of the National Surveillance database. Percentage of new HIV cases with unknown mode of HIV transmission increased from 9.4% in 2009 to 35.0% in 2013.

Methods: Retrospective analysis of the National HIV/AIDS database of the Centre for Communicable Diseases and AIDS was performed. Objective was to assess the trends in unknown mode of HIV transmission in Lithuania from 2009 up to 2013.

Results: In the last five (2009-2013) years 139 HIV cases with unknown mode of transmission were registered in Lithuania. Up to January 1, 2014 (1988-2013), totally 228 cases (10.2%) with unknown mode of transmission were detected. Increasing percentage of HIV cases with unknown mode of transmission was annually observed. In the last five years percentage of new HIV cases with unknown mode of HIV transmission increased from 9.4% in 2009 to 35.0% in 2013. One third (29.5%) of cases with unknown mode of transmission were reported while screening the blood donations, 23.0% - when persons voluntarily applied for testing, 17.3% - in the institutions of imprisonment, 14.4% - among in-patients, 6.5% - during prophylactic testing, 5.0% - while screening the pregnant women, and 4.3% - in other
settings. In 2009-2013, the percentage of new cases with unknown mode of HIV transmission mostly increased among in-patients from 11.8% in 2009 to 20% in 2013.

Conclusions: Increasing proportion of undetected HIV transmission mode suggests insufficient voluntary counseling and testing (VCT) in context of assessing risk behaviour of HIV patients and planning risk behavioural change interventions. Medical staff should improve their knowledge on VCT.
Tick-borne encephalitis in Lithuania, Latvia and Estonia

Abstract No 49

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Categories

4. Seasonal infections: influenza and tick born diseases

Keywords

tick-borne, encephalitis, incidence

Presentation type: Poster

Contact: milda.zygutiene@ulac.lt

Submission date: 2014-03-25 07:45:28

Abstract (english) (2375 characters)

Problem statement. Tick-borne encephalitis (TBE) is among the most important vector-borne diseases of humans in Europe and is currently identified as a major health problem in many countries. TBE endemic zones have expanded over the past two decades, as well as the number of reported cases within endemic areas. The Baltic countries are considered a TBE endemic area with one of the highest incidence rates in the Europe. TBE virus (TBEV) is transmitted by hard ticks of the Ixodes species.

Methods. Ixodes ricinus ticks were sampled from woodlands by the flagging method, dragging flannel flags over the vegetation from different locations of Baltic countries. All collected ticks were placed into tubes and stored alive at 5º C until they were analyzed in pools for the presence of TBEV. All pools were screened with an in-house real-time RT-PCR, and the positive pools were pyrosequenced. Data of morbidity was analysed from official reports of Centre for Communicable Diseases Prevention and Control, Lithuania, Centre for Disease Prevention and Control of Latvia and Infectious Diseases Surveillance and Immunisation Unit Estonian Health Board.

Results. In the eastern areas of Estonia and Latvia, the range of I. ricinus overlaps with I. persulcatus while the main vector of tick borne diseases in Lithuania is I. ricinus. A significant rise of morbidity has been seen in the last two decades. The highest incidence of TBE was registered in 2003 with 763 TBE (22 cases/100000 population) in Lithuania. In 2012 TBE average incidence in Latvia was 18.4, in Lithuania - 16.5 and in Estonia – 13.1/100000. The largest abundance of ticks (52-129 ticks/1 km of road) was observed in the central part of Lithuania. The average prevalence of TBEV in field ticks: Lithuania – 1.3%, Latvia – 6.8%, Estonia – 2.09%. Infection by the alimentary route resulting from consumption of raw milk has been reported in all 3 Baltic countries.
Conclusion. In the Baltic states, recent increases in TBE may have arisen largely from changes in human behaviour that have brought more people into contact with infected ticks. In addition to social, political, ecological, economic, and demographic factors, changing climate conditions may have created more favourable living conditions for ticks and thus led to a further spread of tick-borne diseases.
Review of reasonable influenza vaccination among risk groups in Lithuania, 2012-2013

Abstract (english) (1529 characters)

Background. To comply with recommendations of the European Centre for Disease Prevention and Control of 2007, Lithuania has initiated vaccination of the risk groups against seasonal influenza. Vaccination against seasonal influenza is important to protect people, particularly those of the risk groups, from influenza and its complications.

Methods. By the Order of the Minister of Health, the Centre for Communicable Diseases and AIDS (CCDA) receives monthly reports on seasonal influenza vaccination from 10 territorial public health institutions. CCDA summarizes and submits the report to the Ministry of Health every month and at the end of influenza season performs analysis of influenza vaccination.

Results. In flu season 2012-2013, 95,136 people in the risk groups received free influenza vaccination (6.9% of the Lithuanian population). The highest percent of vaccination coverage was reported among people of 65 years and older – 55.2%, among persons with chronic diseases – 26.6%, and among health care workers – 12.8%. The lowest vaccination coverage was among people who live in social care facilities – 5.3% and among pregnant women – 0.07%.

Conclusions. In comparison with 2012-2013 and 2011-2012 influenza seasons, the risk groups vaccination during 2012-2013 influenza season has considerably increased (2012-2013 – 6.9%, 2011–2012 – 6.4% of all Lithuania population). Increased coverage of vaccination could be the result of active influenza season.
Epidemiological news (HIV, TB, VH and STI) in Lithuania, Latvia and Estonia

Abstract No 51

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Categories
3. HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords
HIV, TB, viral hepatitis, STI, Baltic states

Presentation type : Poster
Contact : ulac@ulac.lt
Submission date : 2014-03-25 14:01:29

Abstract (english) (36 characters)
Overview on the epidemiological situation with HIV, TB, viral hepatitis and sexually transmitted diseases in Lithuania, Latvia and Estonia (conference opening).
Impact of migrants on the spread of HIV-1

Abstract (english) (1357 characters)

Migration flows have a large impact on the spread of HIV infection. There are 11,100,000 foreign citizens staying in the Russian Federation as of the end of 2013. Over 1.2 million blood samples of foreign citizens are tested for HIV antibodies every year. Over 20,000 HIV positive foreign citizens have been detected in the Russian Federation since 1985. Worryingly, that of the total number of HIV-infected migrants registered in Russia, more than half have been identified in the capital. The example of Moscow can consider what impact migrants on the epidemiological situation of HIV infection. According to the operational monitoring of all the territory of Moscow residents account for 58% of the total number of HIV-infected people identified in Moscow, 30% - people in other regions of the Russian Federation, 8% - foreign nationals, 4% - persons homeless.

In Russia, the highest rate in the world survey population for HIV antibodies. Annually in the Russian Federation for HIV surveyed about 17-18% of the population. Together with the mandatory submission of the information from laboratories in AIDS centers, and from the AIDS centers at the federal level, we are able to see the objective epidemiological situation in the country.

Thanks to the timely adoption of preventive measures, the situation with HIV in Moscow was stabilized.
Vertical transmission of HIV infections in twins

Abstract No 53

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Categories
HCV, HBV, HIV and TB: Epidemiology & Diagnostics

Keywords
HIV, vertical transmission, twins

Presentation type: poster
Contact: Tatjana.kolupajeva@aslimnica.lv
Submission date: 2014-03-18 15:38:49

Abstract

Background and Aims
In Latvia the first case of HIV transmission was registered in 1998. On January the 1st, 2014, number of HIV infected children aged 1m. - 16y.o. was 59. Advanced HIV disease in mother associated with likelihood of transmission to infant. It is known that twins born first are at higher risk of HIV infection. Aim of study was to analyze the cases of twins born to HIV-1 infected mothers enrolled in care in Latvian Center of Infectious disease (2007-2013).

Material and Methods.
We investigated 9 twin pairs, who were born in 2007-2013 (in
2007-1, 2010-1, 2012-2, 2013-5). Through Caesarean section delivered 7 twins, vaginally – 2, sex identical were 6 pairs (boys – 2, girls – 4). For diagnoses of HIV infection in infants ELISA kits for the detection and confirmation of HIVp24 core Ag (Innotest) and rt-RT PCR kit (Cobas AmpliPrep/TaqMan HIV-1 system, Roche) for HIV RNA detection (detection limit 20 cop/ml) and quantification were used. CD4+ cell count were detected by flow cytometry. Third generation MEIA assay (ABBOTT) was used for the demonstration of anti-HIV seroreversion in uninfected infants.

Results: The first twin pair was presented to hospital in 2007, then 1 and 2 in 2010 and 2012 accordingly. Significant increasing of twins (5) born to HIV-1 infected mothers was observed in 2013. Prematurity (31-37 weeks) of deliveries observed in 89% (8/9) and maternal age >30 (56% - 5/9) were regarded as a risk factors. Mother’s viral load was from undetectable (2/9 – 22%) to 10^5 cop/ml (1/9 – 11%), more often (6/9 – 67%) from 10^2 (min- 5.9 10^2) to 10^4 (max- 7.7 10^4), CD4+ - from 174 to 816 cells/mm^3, only in 1 (11%) > 700, as an additional risk factor - in 3(3/9 – 33%) < 500 cells/mm^3 (174- 396).

Five HIV-1 infected mothers received antiretroviral therapy (2 – from 14 weeks of pregnancy, others – from 23, 25 and 30 week), four didn’t. At time of first visit (as a rule at age 5 - 9 weeks, 1 twin – at 10 month) all 18 infants have negative HIV-1 Ag and 16/18 (89%) - undetectable level of HIV viral load. Two first born children from different twins have detectable HIV-1 viral load - 7.2 x10^2 (Caesarean section) and 1.2x10^5 cop/ml (vaginally delivery), one was born to mother who didn’t receive antiretroviral therapy, the other – to mother who began ART at week 25 of gestation. The rest infants hadn’t detectable HIV RNA and HIV antibody in age 14-24 m. or till now are on follow up with no detectable HIV RNA and seroreversion trend in levels of HIV antibodies.

Conclusion: Number of twin deliveries from HIV-1 infected mothers increased in Latvia, like in other industrial countries. Recently vertical HIV transmission is proved in 2/18 infants from twin pairs, both first born to mothers, which didn’t receive antiretroviral therapy. Most twin’s mothers have one or more vertical transmission risk factors (age, born prematurity, viral load, CD4+ count).
Identification of an informative and accurate region of HCV genome for phylogenetic analysis

Abstract (english) (3459 characters)

One of the goals of the Baltic Network Against Life-threatening Viral Infections is to gain insights into the joint evolutionary and epidemiological behaviour of hepatitis C virus (HCV) infection (phylodynamics) in the Baltic area. By incorporation of tools from the field of phylogenetics, a number of fundamental questions regarding viral spread and epidemiological dynamics can be addressed. To facilitate collaboration between the different teams of the Network, criteria for inclusion of patient samples, selection of a suitable genomic region for analysis and a PCR amplification strategy is needed. Previous studies have shown that the commonly sequenced region of NS5B is suitable for genotyping and molecular epidemiology studies, however, other regions may also be optimal for phylogenetic analyses. The goal of this study was to 1) identify informative HCV regions that allow for accurate reconstruction of the “true” HCV phylogeny, including identification of “correct” and “statistically supported” clusters, and 2) suggest a
convenient PCR and sequencing protocol suitable for the general molecular biology laboratory. The study used the statistical Shimodaira-Hasegawa (SH) test to compare phylogenetic trees obtained from 7 regions (1236 bases of E1-E2, 933 bases of E2, 1455 bases of E2-NS3, 1272 bases of NS5A, 2934 bases of NS5A and NS5B, 1668 bases of NS5B and 640 bases of NS5B) to the near full-length genome alignment (9036 bases) representing the polyproteins of HCV. In this investigational study, all sequence regions were derived from a set of 143 HCV-1a genomes available in the Los Alamos HCV database. Maximum-likelihood (ML) trees and SH branch-support of internal branches (N=141) of each region were estimated and compared to the “true tree” obtained from the polyprotein region. Inconsistency of tree topologies of shorter regions was statistically compared to the “true tree”. False positive (FP) branches were defined as statistically supported branches (SH > 0.9) of trees obtained from subgenomic regions that were absent or lacked statistical branch support in the phylogeny of the polyprotein region. In total, 75, 35, 28, 26, 22, 18 and 8 branches of the polyprotein, NS5A-NS5B, E1-E2, NS5B, NS5A, E2-NS3, E2 and short-NS5B regions, respectively, displayed statistical support by the SH test as implemented in PhyML. The lowest FP rates were observed in the NS5A, E2-NS3 and E2 regions (15, 22 and 23%, respectively), whereas the FP rates in the NS5A-NS5B, E1-E2, NS5B and short-NS5B regions when tested by this ML-method were higher (37, 39, 46 and 65%, respectively). Among trees obtained from different regions, the NS5A and NS5A-NS5B maintained a phylogeny most similar to the full-coding polyprotein. In summary, we show that the 1272-bp region of NS5A displayed the lowest FP rate among subgenomic regions investigated in this study and conformed a topology of the “true” tree. In comparison to full-length genome sequencing, the NS5A fragment represents a trade-off between phylogenetic accuracy/information content and feasibility in terms of convenient PCR and sequencing protocols. Thus, the NS5A region may represent an attractive target for phylogenetic and phylodynamic studies of HCV. We are currently underway to confirm our findings with other statistical methods and HCV subgenotypes, and to optimize broad and/or subgenotype specific PCR and sequencing protocols for different HCV subgenotypes.