ents respectively. 20% of women had Depressive episode (F32). Adjustment disorders (F43) were found in 32,3% of patients. Personality disorders (F60) and mental disorders due to brain damage (F06) were found in 15,4% and 13,9% of patients respectively. Cognitive impairment was found in 43,1% of patients and was characterized by mild cognitive disorders (asymptomatic neurocognitive impairment in Antinori A. [et al.] classification). Patients with cognitive impairment were characterized by visuospatial agnosia, visuomotor memory and coordination impairment, intellectual impairment with the decline in abstraction ability.

No difference in the level of cognitive impairment between HIV-infected patients with early syphilis and HIV-infected patients with early neurosyphilis was identified. The presence of cognitive impairment was significantly associated with lower counts of CD-4 lymphocytes in the blood (343,53±223,93 and 506,38±221,96; p=0,038; R=-0,36, p=0,031). The severity of HIVassociated neurocognitive disorders (HAND), according to the BNCE test results, was linked to the following factors: hepatitis C coinfection (R=-0,38, p=0,003), substance abuse (R=-0,39, p=0,002) and intravenous drug use (R=-0,51, p<0,0001). Correlations between HAND and brain injuries, stage of HIV infection, time elapsed after being infected and viral load in the blood were not identified. Cognitive impairment in patients without mental disorders was found significantly less frequently (R=0,58; p<0,001). HAND were associated with mental disorders due to brain damage (R=-0,93; p<0,0001), dependence on stimulants (R=-0,69; p=0,014), opiate dependence (R=-0,48; p<0,001), and dependence on alcohol (R=-0,28; p=0,037). Patients with adjustment disorders were less likely to suffer from cognitive impairment (R=0,27; p=0,047). Social adaptation of patients with HAND was often assessed as low (R=0,47, p<0,001).

*Conclusions.* Cognitive impairment occurs in 43% of HIV-infected patients with early syphilis; it is more common in patients with comorbid mental disorders (mental disorders due to brain damage and addictive disorders) and affects their social adaptation. Its manifestations include visuospatial agnosia, intellectual impairment and visuomotor memory and coordination impairment. Early neurosyphilis has no effect on clinical manifestations of HAND.

### Developing a technology for the early diagnostics of bacterial and fungal opportunistic infections in HIV patients

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This report presents the results the study looked into 66 patients who were hospitalized in the Infectious Disease Department with diagnosed HIV-infection in stages 2B and further. The control group comprised 33 people who were examined and divided into health groups I and II. Microorganisms were identified by means of standard methods: bacterial swab test with application of selective growth medium, as well as using sensitivity of a given isolates to oxacillin, optochin, or bilis. Serotype *Streptococcus pneumoniae* was identified and defined by way of multiplex PCR. Microorganisms were isolated from swabs taken in the throat and nose, sputum, pleural fluid and blood.

Microflora of upper respiratory airways in the main group was represented by the following isolates: fungi *Candida; Staphylococcus epidermidis* and *Streptococcus mitis/oralis; Staphylococcus aureus*, including MRSA (45% of patients); *S. pneumoniae, Haemophilus spp, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa*. The composition of fungi Candida was represented by 4 species: the proportion of Candida albicans, Candida tropicalis, Candida glabrata and Candida krusei. According to the PCR tests, the main serotypes are 6ABC, and representatives of serotype 10A.

In the control group, gram-positive cocci prevailed: *Staphylococcus hominis, Micrococcus spp, S. aureus, Staphylococcus epidermidis*. Fungi *Candida, Proteus mirabilis, K. pneumoniae* and *Acinetobacter spp*.

The fact that the mucous membranes of the upper respiratory airways are colonized by flora of bacterial in HIV-positive patients can facilitate diseases caused by these microorganisms, therefore, such patients require routine observation, prescription of ART and taking antibacterial preventive measures against opportunistic infections already at the latent stage of the disease. HIV-positive patients shall have early specialized preventive treatment for the mentioned infections (vaccination).

### Skin explant model for optimization of delivery of genetic vaccines and gene-based drugs

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*Background:* Electroporation (EP) is one of the most efficient approaches when in comes to intradermal gene delivery. The method has been known to enhance gene delivery and subsequent in vivo expression by 100–1000 fold, and is considered as crucial technique for delivery of therapeutic genes including CRISP gene editing. Today, there is also a definitive evidence showing increased efficacy of gene immunization as compared to classical vaccine techniques. The efficacy of this technology in large animals is secured by electroporation-mediated gene delivery. Technologies and methods for gene delivery have been rapidly developing in the past few

decades. A wide array of available electroporators and electrodes available today require careful evaluation and optimization for different applications. The process can be demanding and involves the use of large number laboratory animals for preclinical testing. Objectives: We have adopted the use of a skin explant model to optimize the delivery of plasmid DNA using intradermal injections followed by electroporation.

*Methods:* Skin explants were obtained from mice, non-human primates collected post-mortem from marmosets euthanized in unrelated trials, or humans represented by aborted material after cosmetic operations, Skin explants were cultured in a humidified $CO_2$ incubator for up to 72 hours. The explants were injected intradermally with a DNA plasmid encoding a near-infrared fluorescent reporter protein (iRFP670). The explanted skin was immediately electroporated using either a 2-needle, multi-needle array, plate or fork-plate electrode utilizing varying pulse voltages (50V, 75V, 100V) and pulse polarities (+/-, +/+) (BEX Ltd, Japan). Expression of the DNA construct was monitored daily using a Spectrum CT device (Perkin Elmer) to quantify the fluorescence generated by iRFP670. At the end of the culturing period crawl-out cells emigrating from the tissue were collected, counted and evaluated for cell type and the efficacy of direct transfection/reporter expression using flow cytometry.

*Results:* Injection of the fluorescent reporter with subsequent electroporation resulted in observable expression indicated by up to 16-fold increase of baseline fluorescence intensity 3 days post immunization. Efficiency of DNA delivery/reporter expression was evaluated by the detected fluorescence and depended on the type of electrode, voltage and amount of DNA used. Fifteen micrograms or less resulted in fluorescence levels similar to the background regardless of the electrodes, parameters or species used. A dose of 30 μg DNA was sufficient to quantify the signal with good precision. As low is 300 ng of the reporter protein could be detected in the skin, and also *in vivo*, in injected animals, starting from 24 h post injection of 30 μg of the reporter gene. Using this amount, we observed the highest expression levels when electroporating with fork-plate electrode, followed by plate, multi-needle and 2-needle. Driving pulses of 70–70 volts were optimal for efficient expression and induced low levels of tissue damage. Too low (50V) voltage did not yield considerable expression. High voltage (>100V) supported similar expression levels to those after 75V electroporation, but resulted in more tissue trauma. Delivery of the driving pulses of the same (+/+) versus alterating (+/-) polarity demonstrated no enhancement of reporter expression due to electric field alterations. Methodology has been applied for optimization of delivery of immunotherapeuticals based in plasmids encoding drug-resistant HIV-1 enzymes, for prevention of drug resistance in HIV-1/AIDS.

*Conclusions:* The skin explant model seems to be a promising alternative to animal preclinical and even human testing of delivery of gene therapeuticals and genetic vaccines. Gene delivery can be significantly enhanced by optimized electroporation. Skin model allows such optimization. It is easy to work with, provides quick feedback of delivery efficiency when using a reporter gene, and considerably reduces the number of animals required for optimization of gene delivery. Study was in part supported by Russian Science Foundation 15-15-30039, and Thematic partnership of the Swedish institute grant 09272/2013.

**Role of gut microbiota in microbial translocation: in HIV-infected patients**

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Bacterial components, passed to the bloodstream from the gut as a result of microbial translocation, is known to induce immune hyperactivation causing progression of HIV infection. However, the pathogenesis of this process is not fully understood.

*Hypothesis.* Qualitative and quantitative gut microbiota abnormalities lead to intensification of microbial translocation.

*Objective.* To estimate the impact of intestinal flora abnormalities on concentration of serum markers of the microbial translocation in HIV infected patients, and compare these values with the clinical data.

*Materials and methods.* A cross-sectional study will be carried out in 120 ARV-naive HIV-positive subjects at different stages of the disease.

Gas chromatography mass spectrometry will be used to evaluate microbiota of small and large intestine. To assess colon bacterial population stool cultures for potential pathogens also will be done. Microbial translocation will be analyzed through serum levels detection of endotoxin, 16s ribosomal DNA and soluble CD14.

The data obtained will be compared with the clinical and laboratory characteristics.

*Expected Results.* The findings extend the understanding of the gut microbiota's role in microbial translocation mechanisms in HIV-infected individuals. Furthermore, research forms basis for pathogenetic correction of some gastrointestinal symptoms and disease progression.

**Co-infection of the human placenta and problem of the mother-to-child transmission of HIV A**

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*Background:* The mother-to-child transmission of HIV in the absence of any interventions transmission rates range from 15–45%. This rate can be reduced to levels