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PERINATAL LISTERIOSIS: THE MOUSE MODEL

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The Gram-positive bacterium *Listeria monocytogenes* is typical sapronontic pathogen. *L. monocytogenes* causes listeriosis, a severe disease with multiple manifestations including stillbirths and meningitis of newborns, in humans and a wide range of domestic and wild animals. The invasion factor of the internalin family InlB is involved in crossing the maternal-fetal barrier (Disson et al., 2008). Previously, we compared human and wild animal *L. monocytogenes* strains and described several naturally occurring InlB variants. We demonstrated that InlB variants differed in the ability to support intragastric infection in mice (Sobyanin et al., 2017). The aim of this work was to compare effects of InlB variants on perinatal infection. The mouse model was used. The InlB variants differing in 10 amino acid substitutions were expressed under the same promoter in the *L. monocytogenes* strain EGDeΔinlB. Work with animals was performed with approval of local bioethical committee. Mice were intragastrically infected on the 14th day of pregnancy, euthanized 1 and 3 dpi, bacterial loads were determined by plating. One of two InlB variants provided infection of both placentas and fetuses while another did not. Bacteria carrying InlB variant 14 but not the variant 9 were revealed in placentas 24 and 72 hpi. 65% of placentas and only 20% of fetuses were infected. Fetus infections was correlated with placenta infection. Infection was unequal for different fetuses in the same animal with bacterial loads ranges from individual bacteria to 10^5 CFU per fetus. Obtained results suggested that some but not all InlB variants might promote perinatal infection upon intragastric infection and that the infection of each placenta happens individually.

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PHENOTYPES AND GENOTYPES OF CLASSICAL AND HYPERVIRULENT *KLEBSIELLA PNEUMONIAE* CLINICAL STRAINS ISOLATED IN MOSCOW IN 2013–2018

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Klebsiella pneumoniae is causative agent of community-acquired and healthcare-associated infections including pneumonia, bloodstream infection, surgical site infections, liver abscess and meningitis. Multidrug resistant (MDR) *Klebsiella* belonged to classical branch of *K. pneumoniae* (cKp) have been included recently into the ESKAPE group of pathogens. On the other hand, in the last two decades hypervirulent *Klebsiella* phylogenetic branch (hvKp) emerged and spread around the world. In this study, we aimed to investigate phenotypes and genotypes of virulence and antibacterial resistance for 500 *K. pneumoniae* clinical strains collected in 2013–2018 from the patients of several Moscow hospitals.

Virulence factors and antibiotic resistance profiles between classical and hypervirulent *K. pneumoniae* isolates were compared. It was shown that hvKp strains were attributed to international sequence types ST23, ST86, ST65, and to novel clones ST2174 and ST2280, while strains of cKp — to international clones ST218, ST395, ST11, ST39, ST48, ST147, ST833, ST20, ST13, and ST3346. All hvKp strains had hypermucoviscosity phenotype, capsule types of K1, K2 and K57; carried 5–7 pathogenic genes (regulator of mucoid phenotype gene *rmpA*, aerobactin gene *aer*, iron uptake system gene *kfu*, allantoin metabolism gene *allR*, lipopolysaccharide synthesis genes *uge2* and *wabG*, and fimbrial gene *fimH*). On the contrary, cKP strains had no hypermucoviscosity phenotype, identified capsule types were K57, K62, K47, K14, K27, K28, K60, and K420. Such strains carried four or less pathogenic genes (they did not have *rmpA*, *aer*, and *allR* genes).

Major cKP strains in this study expressed the MDR phenotype, resistance to three or more classes of antibacterials; while more than 50% of them were resistant to six or more classes (beta-lactams, aminoglycosides, fluoroquinolones, sulfonamides, nitrofurans, phenicols). Molecular mechanisms of MDR include beta-lactamase genes (bla_{TEM}, bla_{SHV}, bla_{CTX-M}, bla_{OXA}, and bla_{NDM}), class 1 integrons carrying gene cassettes (*dfr, aac, aad,, aph,* etc.), and efflux pumps (*oqxAB, mph, cml,* etc.). Among hvKp strains two groups were described: (1) most of them were mainly susceptible to antibacterials carrying few resistance genes, (2) some strains accepted MDR plasmids carrying resistance genes, and expressed MDR phenotype.

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RELATIONSHIP BETWEEN MICROORGANISMS IN THE VAGINAL BIOTOPE OF SUBFERTIL WOMEN

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The aim of investigation was to evaluate the features of microecology of the lower genital tract of women with infertility.

A retrospective analysis of microbiological data of the vaginal discharge of 345 subfertil women was carried out. To assess the share of different types of microorganisms in the structure of the microbiota the coefficient of species constancy was used. To quantify the interaction between members of the microbiocenosis, the Jacquard similarity coefficient was used.

The nature of the relationship between the main members of the microbial community in the vaginal biotope of women with infertility should be considered antagonistic. The phenomenon of mutualism was characteristic only between *Lactobacillus* spp. and *Peptostreptococcus* spp. Typical *E. coli* have a significant ecological community with these bacteria, the relationships of their can be characterized as synergistic. Similar ecological synergism was revealed for *S. epidermidis* and lactobacilli. It was shown that in subfertil women *E. coli* acquires the functions of stabilizing strain and its activity often associated with both a change in the species composition of lactobacilli and their functional characteristics. In a similar situation despite the prevalence of microbial antagonism in the vaginal microbiota, *Lactobacillus* spp. "admit" the existence of *E. coli*, *Enterobacter* spp., *S. aureus*, *S. epidermidis*, *S. haemolyticus*, *S. agalactiae*, *Enterococcus* spp. and *C. albicans.* Under such conditions, the negative influence of commensal microorganisms on lactobacilli is enhanced and its have manifestation by a marked decrease in their numbers and functional activity, as well as a decrease in the sensitivity of the associates to the biocidal factors of lactobacilli when coexisting.