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Raita Stefania Mariana, J Infec Dis Treat 2018, Volume 4
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Histological examination of a Yorkshire pig line for SCID-like occurring individuals

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The severe combined immunodeficiency (SCID) in pigs has been recently reported beneficial for development of animal model for human research, especially for preclinical testing of potential cancer treatment. Immuno-compromised animal models can be used for successfully hosting the growth of xenografted human tumors, and serve as effective animal model for cancer therapy. Spontaneous occurrence of SCID-like defects has been reported as common in intensively selected breed lines. This study aimed to screen a population of Yorkshire pigs selected for feed efficiency, from a private holding with reported increased morbidity and mortality, in order to assess the SCID-like occurrence rate. SCID animals are valuable biomedical models and can be used for scientific purposes. In total, 20 randomly selected piglets from 15 litters were processed for blood sampling, as well as thymus and lymph node tissue samples collection. Blood samples were analyzed for lymphocyte number, while the thymus and lymph node samples were histologically examined for atrophy signs. Six piglets (30%) tested positive for low lymphocyte count, atrophied thymus and lymph nodes, while five piglets (25%) tested positive for either one/two of the three considered examinations. Based on these results it can be hypothesized that the immunodeficiency phenotype is affecting the selected line of pigs in the population. The identification of spontaneously occurring SCID-like defects in pigs is beneficial for research institutes and for the owner of the holding, who can find a destination for affected individuals and redirect animal selection to obtain defect-free individuals.

Biography

Raita Stefania Mariana has completed her PhD from University of Agronomic Sciences and Veterinary Medicine of Bucharest, Romania. She is Lecturer within the Veterinary Medicine Faculty of Bucharest and the Coordinator of the Histology and Embryology Discipline for the Veterinary Medicine Romanian Program and the Veterinary Medicine French Program. She has published over 60 scientific papers in reputed journals and has been involved as member of the research team, or project coordinator in numerous research grants. Her research interests lies in animal and human histology and embryology, histopathology and cytology.

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Raita Ştefania Mariana, J Infec Dis Treat 2018, Volume 4
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Histological examination of meat products, for quality and adulteration screening

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The quality of meat products is fully and more accurately assessed when histological examination is considered in addition to physicochemical and microbiological evaluation. The histological examination of cured meat products enhances the amount of information on the quality of the raw material, by identification of the animal tissue content, helping in detecting fraud. In Romania, cured meat sausages are marketed as first quality products and target a specific consumer category, selected by the price range. This study aimed to evaluate the quality of cured meat sausage of three popular Romanian meat products producers. Thirty samples (ten from each producer) of the same cured meat sausage assortment were fixed in 10% neutral buffered formalin and routinely processed for paraffin embedding. Three histological sections of each sample were stained with Cajal's triple stain method, modified by Calleja's variation. Each section was examined for animal tissue types. The evaluation showed similar skeletal muscle/adipose tissue ratios for all examined samples, specific for the type of meat product under assessment. In addition to skeletal muscle tissue, adipose and connective tissues, and blood vessels, the evaluation revealed the following tissues: cartilage, nerve, glandular and bone tissue. No significant differences were noticed between the occurrence rates of undesirable tissue, between producers, but the average number of positive samples (30% for glandular tissue and 16.67% for bone tissue) exceeds the technologically unavoidable frame. These results indicate that histological examination should be considered for routine meat product quality assessment and adulteration screening.

Biography

Raita Ştefania Mariana has completed her PhD from University of Agronomic Sciences and Veterinary Medicine of Bucharest, Romania. She is Lecturer within the Veterinary Medicine Faculty of Bucharest and the Coordinator of the Histology and Embryology Discipline for the Veterinary Medicine Romanian Program and the Veterinary Medicine French Program. She has published over 60 scientific papers in reputed journals and has been involved as member of the research team, or project coordinator in numerous research grants. Her research interests lies in animal and human histology and embryology, histopathology and cytology.

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Tarek Mohamed Kamal Mohamed Metawie et al., J Infec Dis Treat 2018, Volume 4
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Molecular association of lncRNA-uc003wbd and lncRNA-AF085935 expression with a genetic variant profile in Egyptian patients with hepatocellular carcinoma and HBV

Tarek Mohamed Kamal Mohamed Metawie, Shohda Assem El-Maraghy, Dina Sabry Abdel Fatah and **Noha Ali Mehana**
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Hepatocellular carcinoma (HCC) was among the most common solid tumors, rated third in cancer-related mortality worldwide. The burden of HCC has been increasing in Egypt with a doubling in the incidence rate in the past 10 years. This has been attributed to several biological (e.g. hepatitis B (HBV) and C (HCV) virus infection) and environmental factors. HBV infection is of particular interest, for its coherent distribution with the HCC prevalence. Thus, new diagnosis measures and targeted treatments for HCC and HBV are in need. Long non coding RNAs (lncRNAs) are dysregulated in different cancers and have critical roles in various biological processes such as HULC and MALAT1 may participate in HCC development and progression. Besides, considerable studies have investigated the effects of lncRNAs genetic variations on cancer susceptibility. Through this study, we aimed at exploring the expression profile and the potential clinical value of two lncRNAs (lncRNAuc003wbd and lncRNA-AF085935) in differentiating HCC from both HBV patients and the healthy specimens and their associations with single nucleotide polymorphisms (SNPs) in HULC and MALAT-1 and the susceptibility to HBV chronic infection and HCC. Serum samples were extracted from 70 HBV patients, 70 HCC patients, and 70 healthy controls. The level of serum lncRNA-uc003wbd and lncRNA-AF085935 of all the subjects were assayed by quantitative real-time reverse transcriptase polymerase chain reaction (qRT-PCR). Moreover, we have genotyped two SNPs, rs7763881 in HULC and rs619586 in MALAT1, in all subjects to test the association between the two SNPs and susceptibility to HCC and HBV chronic infection. The level of serum lncRNA-uc003wbd and lncRNA AF085935 was significantly upregulated in HCC patients and HBV patients compared with that in normal controls. The variant genotypes of rs7763881 were significantly associated with decreased HCC risk. Similarly, variant genotypes of rs6682925 were associated with non-significant decreased HCC risk compared with the wild-type AA genotype. However, no significant association was found between the two SNPs and HBV clearance. In conclusion, our results showed that both lncRNAuc003wbd and lncRNA-AF085935 are able to be potential biomarkers for HCC and HBV screening as well that SNP rs7763881 in lncRNA HULC was significantly associated with the decreased susceptibility to HCC in HBV persistent carriers.

Biography

Tarek Mohamed Kamal Mohamed Metawie is a Professor of Biochemistry in the Faculty of Pharmacy, Cairo University. He has completed his PhD in Pharmaceutical Sciences in 1984; MSc in Pharmaceutical Sciences in 1979; BSc in Pharmaceutical Sciences in the Faculty of Pharmacy at Cairo University in 1976. Professional experience: Instructor; 1976, Lecturer Assistant; 1980, Lecturer, 1984; Assistant Professor, 1989; Professor, 1994; Head of the Department of Biochemistry, Faculty of Pharmacy, and Cairo: - 2008-2014.

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Myungjo You et al., J Infec Dis Treat 2018, Volume 4
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Proteomic characterization of *Haemaphysalis longicornis* saliva and determination of saliva-host interaction during blood-sucking periods

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Abstract: *H.longicornis* saliva proteomic profile, role of histamine-antihistamine and cytokines interection with host were design and performed in this work.

Methods: For salivary protein LC-MS/MS was performed. Histamine and antihistamine were administered at different interval to see its effect on detachment during attachment and fast feeding stage, respectively. Histamine concentration was measured by ELISA and differences in expression of genes related to immune response were measred by qPCR.

Results: A total of 135 tick salivary proteins were identified of which 30 proteins were found exclusively in fully engorged nymph saliva, 74 in fully engorged adult females, and 31 were detected in both stages. Ticks exhibited a higher detachment rate (30.1%) 12 hours after histamine application during attachment stage and antihistamine injection (25.44%) at 96 hours during fast feeding stage. There is an average increases in body weight were observed for histamine treated group and decrease in body weight was observed in antihistamine treated *H.longicornis* in compare to control. Blood histamine concentration during fast feeding stage was significantly higher in compare to attachment and no-infested groups. Gene expression of TNFα, IFNγ were significantly ($P<0.05$) decrease in all stages of blood sucking both in nymph and adult ticks, while expression of IL-4, IL-6 and IL-10 were increased 1.3 to 7 folds in adult infesteted rabbits in comapre to non-infested with the exception of IL-6 in nymph infested rabbit. IL-6 significantly decreased in nymph infested rabbits and IL-2 was not expressed in either nymph or adult *H.longicornis* treated rabbit. These data can provide a deeper understanding to the biology of H. longicornis.

Biography

Myungjo You's lab has focused on unveiling how hosts response to hard tick infection. They have used various infectious models to prove host responses upon tick infection. In recent, You's lab has found the saliva from nymph and adult females of Haemaphysalis longicornis: a proteomic study (Parasite & Vectors). Moreover, You's lab is expert on tick and tick-borne disease.

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Molouk Beiromvand et al., J Infec Dis Treat 2018, Volume 4
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Molecular genotyping of *Giardia duodenalis* in preschool children

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Giardia duodenalis is an intestinal flagellated protozoan that infects humans and several animal species. Based on molecular studies mainly targeting the small subunit (SSU) rRNA gene locus of the parasite, 8 assemblages (A to H) have been identified in humans and other animal species. The aim of the current study was to evaluate the frequency and molecular diversity of *Giardia* in pre-school children from rural and urban day care centers from Behbahan, Southwestern Iran. This cross-sectional study was based on a concentration method for the microscopic detection of *G. duodenalis* in stool samples of 450 children, aged 1-7 years. The survey was conducted from December 2015 to May 2016. PCR-methods targeting the SSU rRNA and triose phosphate isomerase *(TPI)* genes of *G. duodenalis* were used for the identification and genotyping of the parasite isolates. Based on sucrose flotation and microscopy techniques, 2.7% (12/450) of children were infected with G. duodenalis, of which six (50.0%) were males and the other six (50.0%) were females. Overall, 91.7% (11/12) of the infections were detected in children from rural areas. The SSU rRNA and TPI genes were amplified successfully in nine and eight, respectively of the Giardia-positive samples at microscopy. Among the eight TPI sequences, assemblage A, sub assemblage AII, was identified in five of the isolates. The sequences of the three remaining samples were untypable. Although no significant statistical difference between genotype and clinical symptoms was found, five out of the eight isolates identified as assemblage A were obtained in asymptomatic children. *Giardia* infections were more prevalent in children from rural day care schools and the predominant assemblage was A, sub-assemblage AII. The higher prevalence of giardiasis in rural areas might be related to differences in personal hygiene habits, parents' education level, source of drinking water and inadequate hygienic toilet facilities in rural areas.

Biography

Molouk Beiromvand has completed her PhD at Tehran University of Medical Sciences, Tehran, Iran. She is an Assistant Professor in the Department of Parasitology, School of Medicine at Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

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Seong Kug Eo et al., J Infec Dis Treat 2018, Volume 4
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Blocking 4-1BB signal ameliorates the progression of Japanese encephalitis via divergent type I innate responses

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Japanese encephalitis (JE), a neuroinflammation caused by zoonotic JE virus, is the major cause of viral encephalitis worldwide and poses an increasing threat to global health and welfare. To date, however, there has been no report describing the regulation of JE progression using immunomodulatory tools for developing therapeutic strategies. We tested whether blocking the 4-1BB signaling pathway would regulate JE progression using murine JE model. Infected wild-type and 4-1BB-knockout (KO) mice were examined daily for mortality and clinical signs and neuroinflammation in the CNS was evaluated by infiltration of inflammatory leukocytes and cytokine expression. In addition, viral burden, JEV-specific T cell and type I/II IFN (IFN-I/II) innate responses were analyzed. Blocking the 4-1BB signaling pathway significantly increased resistance to JE and reduced viral burden in extraneural tissues and the CNS, rather than causing a detrimental effect. In addition, treatment with 4-1BB agonistic antibody exacerbated JE. Furthermore, JE amelioration and reduction of viral burden by blocking the 4-1BB signaling pathways were associated with an increased frequency of IFN-II-producing NK and $CD4^+$ Th1 cells as well as increased infiltration of mature Ly-6Chi monocytes in the inflamed CNS. More interestingly, DCs and macrophages derived from 4-1BB KO mice showed potent and rapid IFN-I innate immune responses upon JEV infection, which was coupled to strong induction of PRRs (RIG-I, MDA5), transcription factors (IRF7) and antiviral ISG genes (ISG49, ISG54, ISG56). Further, the ablation of 4-1BB signaling enhanced IFN-I innate responses in neuron cells, which likely regulated viral spread in the CNS. Finally, we confirmed that blocking the 4-1BB signaling pathway in myeloid cells derived from hematopoietic stem cells (HSCs) played a dominant role in ameliorating JE. In support of this finding, HSC-derived leukocytes played a dominant role in generating the IFN-I innate responses in the host.

Biography

Seong Kug Eo's lab has focused on unveiling how hosts response to pathogen infection. They have used various infectious models to prove host responses upon pathogenic infection. In recent, EO's lab has found the detailed pathway that IFN-I signal pathway orchestrated environments to provide effective protection against mucosal viral infection (PLoS Pathog., 2016). Moreover, EO's lab is expert on viral acute encephalitis caused by flaviviral infection.

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Indispensible role of TLR2 and TLR9 in regulating protection against mucosal infection with herpes virus through maturation of Ly-6Chi monocytes and NK cells

Seong Kug Eo[1], **Erdenebileg Uyangaa**[1], **Jin Young Choi**[1], **Ajit Mahadev Patil**[1], **Ferdaus Mohd Altaf Hossain**[1], **Seong OK Park**[1], **Bumseok Kim**[1] and **Koanhoi Kim**[2]
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The importance of TLR2 and TLR9 in the recognition of infection with herpes simplex virus (HSV) and HSV-caused diseases has been described, but some discrepancies remain concerning the benefits of these responses. Moreover, the impact of TLR2/9 on innate and adaptive immune responses within relevant mucosal tissues has not been elucidated using natural mucosal infection model of HSV. Here, we demonstrate that dual TLR2/9 recognition is essential to provide resistance against mucosal infection with HSV via an intravaginal route. Dual TLR2/9 ablation resulted in the highly enhanced mortality with exacerbated symptoms of encephalitis compared to TLR2 or TLR9 deficiency alone, coinciding with highly increased viral load in CNS tissues. TLR2 appeared to play a minor role in providing resistance against mucosal infection with HSV, since TLR2-ablated mice showed higher survival rate compared with TLR9-ablated mice. Also, the high mortality in dual TLR2/9-ablated mice was closely associated with the reduction in early Ly-6Chi monocyte and NK cell infiltration in the vaginal tract, which was likely to correlate with low expression of cytokines and CCR2 ligands (CCL2, CCL7). More interestingly, our data revealed that dual TLR2/9 recognition of HSV infection plays an important role in the functional maturation of TNF- and iNOS-producing dendritic cells (Tip-DCs) from Ly-6Chi monocytes as well as NK cell activation in vaginal tract. TLR2/9-dependent maturation of Tip-DCs from Ly-6Chi monocytes appeared to specifically present cognate Ag, which effectively provided functional effector CD4$^+$ and CD8$^+$ T cells specific for HSV Ag in vaginal tract and its draining lymph nodes. TLR2/9 expressed in Ly-6Chi monocytes was likely to directly facilitate Tip-DC-like features after HSV infection. Also, dual TLR2/9 recognition of HSV infection directly activated NK cells without the aid of DCs through activation of p38 MAPK pathway. Taken together, these results indicate that dual TLR2/9 recognition plays a critical role in providing resistance against mucosal infection with HSV, which may involve a direct regulation of Tip-DCs and NK cells in vaginal tract. Therefore, our data provide a more detailed understanding of TLR2/9 role in conferring antiviral immunity within relevant mucosal tissues after mucosal infection with HSV.

Biography

Seong Kug Eo's lab has focused on unveiling how hosts response to pathogen infection. They have used various infectious models to prove host responses upon pathogenic infection. In recent, EO's lab has found the detailed pathway that IFN-I signal pathway orchestrated environments to provide effective protection against mucosal viral infection. Moreover, his lab is expert on viral acute encephalitis caused by flaviviral infection.

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Rainier Mark Alegria, J Infec Dis Treat 2018, Volume 4
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A case report on listeria *monocytogenes* meningoencephalitis, acute disseminated encephalomyelitis, and *cytomegalovirus* viremia in an immunocompromised patient on steroid therapy

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Asian Hospital and Medical Center, Philippines

Introduction: *Listeria* monocytogenes is an opportunistic pathogen that affects immunocompromised patients and has a very high mortality rate. Central nervous system (CNS) infection and bacteremia are the foremost clinical manifestation in susceptible hosts. Infection with multiple pathogens is not common but still possible especially in the immunocompromised.

Case: Presenting a 57-year-old female with chronic kidney disease from probable glomerulonephritis treated with prednisone for 7 weeks. She was admitted for progressive neurologic symptoms that began with Broca's aphasia followed by decreased level of consciousness and fever. There was also concomitant hematochezia. Empiric treatment for CNS infection and pneumonia with intravenous (IV) Ceftriaxone, Vancomycin, Metronidazole, and Acyclovir were given. Lower gastrointestinal bleeding from jejunal angioectasia was treated and resolved. Cerebsospinal fluid (CSF) and blood cultures turned positive for *Listeria* monocytogenes on the 3rd hospital day. Antimicrobial regimen was shifted to Ampicillin and Meropenem. Marked clinical improvement was evident 1-2 days after anti-infectives were shifted. Blood CMV PCR was positive on the 9th hospital day thus IV Ganciclovir was started. Meropenem was shifted to Cefepime and Metronidazole due to progression of pneumonia. On the 16th hospital day, there was recurrence of Broca's aphasia. Non-contrast Brain MRI showed multiple tiny subcortical white matter FLAIR hyperintense foci in the right frontal area with noted low CSF IgG. Acute disseminated encephalomyelitis (ADEM) treatment with Dexamethasone was effective and improved speech production after 3 days. Antimicrobial treatment resolved the infection and the patient was discharged coherent and conversant.

Conclusion: The authors conclude that early detection and treatment of *Listeria* infection is essential for a good prognosis. Infection with multiple pathogens should be watched out for in susceptible hosts. ADEM may develop post CNS infection and should be watched for.

Biography

Rainier Mark Alegria, MD is an Internal Medicine Resident of Asian Hospital and Medical Center. He aspires to improve the quality of health-care in the Philippines by being very active in research and case publication.

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Probiotics for amphibians: Advances in the selection of lactic acid bacteria for chytridiomycosis control

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Statement of the Problem: Chytridiomycosis is an amphibian skin disease caused by *Batrachochytrium dendrobatidis* (Bd) that produces extinction around the world. Some amphibian-skin bacteria have been proposed as probiotic for chytridiomycosis control but they excluded the lactic acid bacteria (LAB) group. Here in, we advanced in the selection of indigenous LAB from bullfrog (considered as a Bd carrier) skin to design probiotic for application during the *ex situ* breeding of endangered amphibians.

Methodology: To determine the anti-Bd activity, co-culture assays between Bd strains (CFLT 159 from Brazil; AVS4 and AVS7 from Chile) and potentially LAB isolates were performed. Isolates previously shown exopolysaccharide (EPS) synthesis and/or auto aggregation (AA) ability were evaluated for biofilm formation by using polyestyrene plates. Compatibility assays were performed to evaluate the possibility to formulate a mixed probiotic.

Findings: From 62 potentially LAB, 48 isolates had any anti-Bd activity. The 16s RNA sequence analysis allowed obtaining 97-99% of identity that matches with *Enterococcus* and *Lactobacillus*. Thus, *Enterococcus* sp. 90, 564, 747, 762; *Lactobacillus* sp. 10, 529, and *Enterococcus* gallinarum CRL 1826 (previously characterized) inhibited all the Bd strains. Three LAB isolates exhibited low biofilm formation, while E. gallinarum showed moderate production. This ability was not always associated with AA or EPS synthesis. The compatibility assays indicated that the LAB isolates could be included in mixed probiotic with the exception of *Enterococcus* sp. 742 that was inhibited by E. gallinarum.

Conclusion & Significance: E. gallinarum CRL 1826 resulted the best strain for a probiotic since it has many beneficial properties: anti-Bd activity, AA, EPS synthesis, biofilm formation, medium hydrophobicity and GRAS properties according to in vitro and in vivo tests (3-7). However, *Enterococcus* sp. 747 would maximize some probiotic properties of the CRL strain; therefore, a mixed probiotic can be proposed.

Biography

Sergio E Pasteris has his expertise in the study of lactic acid bacteria (LAB) metabolism as well as in the isolation and evaluation of its beneficial properties to design probiotics for amphibian culture. Taken into account the development of resistant bacteria, some LAB strains represent an alternative instead chemotherapeutics to prevent epizootics in bullfrog systems breeding. Since bullfrog is a carrier of the etiological agent of chytridiomycosis, probiotics by using native LAB from bullfrog skin are being developed to be applied during the ex situ breeding of endangered amphibian species.

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Sergio E Pasteris et al., J Infec Dis Treat 2018, Volume 4
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Clonal analysis and virulence-associated traits of native *Escherichia coli* from urethra of gilts and natural/artificial pregnant sows

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Statements of the Problem: The reproductive performance of sows is a key factor in the herd´s productivity. Urinary tract infections (UTI) are a common problem in females, causing repeat breeding with a delayed return to estrus, which reduces the animal´s welfare and the litter performance; *Escherichia coli* being associated to these infections. Diverse studies described a unique microbiota in the UT in bitch. Others authors concluded that the composition of the UT bacterial communities could have an important role in the health condition of the host.

Methodology: We performed the isolation and clonal association (rep-PCR, Box and Eric primers) of E. coli from the urethral microbiota of: healthy gilts-HG (n=9) and pregnant sows by natural breading-NB (n=11) or artificial insemination-AI (n=11). Also, 12 virulence factors relevant for pyelonephritic strains were evaluated by PCR: hlyA, cnf, ibeA, iutA, kpsMT II, FimH, papC, sfa/focD, afa/draBC, traT, agn43, csgA.

Findings: Cultures revealed a slightly minor count (CFU/mL) for AI (3.7±0.59) group compared to HG (4.2±0.24) and NB (4.3±0.44). However, there were no differences for E. coli isolation (CFU/mL): 1.45±1.36, 2.87±1.53 and 2.61±1.84, for AI, NB and HG, respectively. The clonal analysis with both, Box or Eric primers, revealed a high similarity (>90%) between E. coli isolates from different animal groups. Positive reaction was found for: FimH (76%), agn43 (92%), traT (32%) and csgA (72%), these last ones showed a differential prevalence and were associated with E. coli from NB sows.

Conclusion & Significance: These results indicate that the management conditions could affect the characteristics of the urethral microbiota in sows and, therefore, the risk for urinary tract diseases.

Biography

Sergio E Pasteris has his expertise in the study of lactic acid bacteria (LAB) metabolism as well as in the isolation and evaluation of its beneficial properties to design probiotics for amphibian culture. Taken into account the development of resistant bacteria, some LAB strains represent an alternative instead chemotherapeutics to prevent epizootics in bullfrog systems breeding. Since bullfrog is a carrier of the etiological agent of chytridiomycosis, probiotics by using native LAB from bullfrog skin are being developed to be applied during the ex situ breeding of endangered amphibian species.

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Sahar F Mansour et al., J Infec Dis Treat 2018, Volume 4
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Interleukin-36α expression in vitiligo skin lesions and its correlation with disease pattern, activity and severity

Sahar F Mansour[1], **Mona A Atwa**[1], **Lina M Atef**[1] and **Rasha Mohamed Ibrahim Mohamed**[2]
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Vitiligo is an acquired multivariate disease, that results in gradual selective degeneration of cells that produce pigmentation in the skin. There is still an ongoing debate about what causes damage to melanin cells and their disappearance from infected skin. Many theories to explain the pathogenesis of vitiligo exist. Recently, one of the autoimmune pathogens theory has been suggested. Interleukin (IL)-36α belongs to interleukin (IL)36-cytokine family, that have a role in organizing non specific as well as acquired immune responses. It is proved that interleukin 36 in many skin disorders, especially autoimmune ones including for example psoriasis. The study will be conducted in an attempt to evaluate interleukin 36α expression using IHC in skin (lesional and non lesional) punch biopsy from vitiligo patients and detect the correlation between interleukin 36α expression with demographic (age, gender,..) and clinical parameters (disease pattern, activity and severity).

Biography

Sahar F Mansour has completed her MD from Suez Canal University, Ismailia, Egypt. She is an Assistant Professor of the Pathology Department of Faculty of Medicine, a premier research organization. She has published more than 10 papers in reputed journals.

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Direct evidence of viral infection and mitochondrial alterations in the brain of fetuses at high risk for schizophrenia

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Background: There is increasing evidences that favor the prenatal beginning of schizophrenia. These evidences point toward intra-uterine environmental factors that act specifically during the second pregnancy trimester producing a direct damage of the brain of the fetus. The current available technology doesn't allow observing what is happening at cellular level since the human brain is not exposed to a direct analysis in that stage of the life in subjects at high risk of developing schizophrenia.

Methods: In 1977 we began a direct electron microscopic research of the brain of fetuses at high risk from schizophrenic mothers in order to finding differences at cellular level in relation to controls.

Results: In these studies we have observed within the nuclei of neurons the presence of complete and incomplete viral particles that reacted in positive form with antibodies to herpes simplex hominis type I [HSV1] virus, and mitochondria alterations.

Conclusion: The importance of these findings can have practical applications in the prevention of the illness keeping in mind its direct relation to the aetiology and physiopathology of schizophrenia. A study of the gametes or the amniotic fluid cells in women at risk of having a schizophrenic offspring is considered. Of being observed the same alterations that those observed previously in the cells of the brain of the studied foetuses, it would intend to these women in risk of having a schizophrenia descendant, previous information of the results, the voluntary medical interruption of the pregnancy or an early anti HSV1 viral treatment as preventive measure of the later development of the illness.

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Presence of *Mycobacterium* and other bacteria in lymphadenopathies with purulent aspirates

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Tuberculosis(TB) is one of the biggest health challenges of the world. TB lymphadenopathy (TBL) is an important site of involvement by extrapulmonary TB. Fine needle aspiration cytology (FNAC) is a cost effective and quick method for diagnosis of such lesions. Although FNAC can offer a definite cytologic diagnosis of TBL in smears with caseaous aspirates, those cases with purulent aspirates may be dismissed as suppurative lymphadenitis unless direct detection of *mycobacterium* performed. The study was aimed to assess presence of Mycobacterium and other bacteria in clinically TB suspected lymphadenopathies with thin purulent aspirates after FNAC performed. The study was conducted from August to December 2017 in patients visiting Jimma University Medical Center (JUMC), South West Ethiopia. Fifty three TB suspected peripheral lymphadenopathy (LAP) cases with purulent aspirates were enrolled and underwent cytomorphologic, LED and ZN staininig evaluation; in which Mycobacterial infection detected in 49%, 43.4% and 9.4% cases respectively. Combining cytomorphology with LED techniques increases the detection rate by 15% when compared with cytomorphology alone while AFB staining increases this detection rate by 7.5%. Gram reaction observed in 17% of cases. We recommend the combined use of routine FNAC with AFB staining and LED techniques to increases the detection of myocobacterial infection in purulent aspirates. Performing Gram stain further help to reveal other bacterial causes of suppurative inflammation.

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Interleukin-36α expression in vitiligo skin lesions and its correlation with disease pattern, activity and severity

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Introduction: Macrocassettes are a very useful tool in the pathology laboratory. Currently, they are usually carried out exclusively in radical prostatectomies. We are pioneers in Spain in using them for all types of tissues. It is not usually known the adequate processing that allows the realization of good quality slides in any type of tissue. The fact that the pathologist can visualize complete structures or larger lesions in a single slide improves efficiency.

Purposes: To present our experience for more than ten years in the fixation, processing, inclusion and cutting of numerous biopsies in macrocassettes (more than 4000) and show the advantages and disadvantages of the use of this technique. Currently, we have launched a practical workshop for pathology technicians teaching these techniques. In this first edition of the workshop we have full occupation from the participants and also we have received numerous emails from professionals from outside Spain to get information to participate.

Equipment & Methods: For more than ten years we have made macrocassettes of all kinds of tissues, bone, kidney, colon, breast, brain with fixings and different processing times, processing the macrocassettes separated from the routine biopsies (due to the time of permanence in each liquid), until obtaining optimal results in each type of tissue. We present our processing protocols and abundant iconography of the process and the results.

Results & Conclusion: The use of macrocassettes facilitates the diagnosis by the pathologist to be able to visualize structures in a more complete way, provide more accurate tumor volumes and more appropriate assessment of surgical edges, automated immunohistochemistry can be performed, collecting from the flotation bath the area that is needed for diagnosis. This technique increases the profitability in the daily work by decreasing the number of cassettes. It's recommended to incorporate this technique to the routine only with a specific processor and qualified technicians in the handling of this type of cassettes.

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JOINT EVENT

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10th Euro-Global Conference on **Infectious Diseases**
&
5th International Conference on **Histopathology & Cytopathology**

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Diagnostic value of conventional fine needle aspiration cytology in cervical lymphadenopathy

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Introduction: Lymphadenopathy is a common clinical presentation in outpatient clinics. Fine needle aspiration cytology (FNAC) of the enlarged lymph node is an easy and simple tool for clinical management. This is because it is fast and minimally invasive with minimal complications.

Aim: To evaluate the reliability and validity of conventional FNAC of cervical lymphadenopathy.

Methods: This prospective study was carried out on 50 patients with cervical lymphadenopathy. The cyto-pathological diagnoses obtained by FNAC were compared with the histopathological results of the ongoing excised nodes.

Results: 54 percent of our cases were females. 74 percent of our cases were less than 40 years. The cytological diagnoses were benign in 29 cases (58%) and malignant (diagnostic or suspicious for malignancy) in 21 cases (42%). The sensitivity, specificity, positive predictive value, and negative predictive value were 84%, 100%, 100%, and 86.2%, respectively. The overall diagnostic accuracy was 92% (46/50), while the overall discordance rate was 8% (4/50).

Conclusions: The overall diagnostic accuracy of FNAC of cervical lymph nodes was 92%. The sensitivity, specificity, positive predictive value, and negative predictive value were 82.6%, 100%, 100%, and 87.1%, respectively. FNAC is a reliable diagnostic tool for the diagnosis of cervical lymphadenopathy.

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Influenza A H1N1 pneumonia in a pregnant lady complicated with acute respiratory distress syndrome: A case study

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Pneumonia is an inflammatory disease of lung parenchyma which is caused by infectious microorganism, bacteria, viruses and fungi. Pregnancy is considered as a risk factor of influenza infection and its related morbidity and mortality. Bacterial pneumonia complicating influenza infection is associated with high morbidity and mortality. The aim of this case study is to present this difficult and complicated case diagnosis and management. Also, we aimed to raise the attention about the team work benefits. This report presents A 39 year's old female patient, pregnant 32 weeks presented with high grade fever associated with cough and breathing difficulty for last three days before admission. Clinically she was diagnosed as pneumonia and she was admitted in ICCU due to hypoxemia. On the second day patient get worse and connected to mechanical ventilation. An elective caesarian section was done in ICCU and baby was shifted to NICU. Swab for H1N1 and corona viruses were done. Results came with influenza A H1N1 was detected and patient was managed as a case of H1N1 community acquired pneumonia complicated with ARDS and respiratory failure. Patient stayed in ICCU on high frequency oscillatory ventilation, received oseltamivir and course of antibiotics. She was discharged after improvement and her baby also was in a good health.

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Preoperative nasopharyngeal decolonization using mupirocin and chlorhexidine in preventing surgical site infection: A meta-analysis

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Background: Preoperative decolonization is a preventive strategy for surgical site infection. Clinical trials have been done to prove or disprove the efficacy of decolonization in the prevention of surgical site infection. However, great heterogeneity in results was noted in many published studies.

Objective: We assessed whether preoperative decolonization reduces the risk of surgical site infection.

Method: PubMed and Google free texts search terms: decolonization and surgical site infection inclusion criteria: >/=18 years old of either gender undergoing any surgery, may or may not screened for carriage of *S. aureus*; studies are randomized controlled trial (RCT).

Results: Using the random effects model, the computed summary statistic was 0.59 with CI 0.37-0.94 in favor of the experimental treatment. However, due to substantial heterogeneity (Tau2 of 0.25 Chi2 30.34 and I2 of 84%), we cannot draw definite conclusion from the meta-analysis. Subgroup analysis using both mupirocin nasal swab and chlorhexidine gargle were used for preoperative decolonization, the summary statistic generated was 0.40 with 95% CI of 0.23-0.69, with no heterogeneity (Tau2 of 0, Chi2 of 0.09 and I2 of 0.) and was noted to be in favor of the experimental treatment.

Conclusion: Pre-operative decolonization using both mupirocin and chlorhexidine for preoperative decolonization showed that it could significantly prevent surgical site infection.

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A study on genomic diversity of norovirus using deep sequencing approach

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A study on genomic diversity of norovirus using deep sequencing approach: Norovirus (NoVs) are the leading cause of epidemic and sporadic gastroenteritis outbreaks worldwide affecting across all age groups, responsible for approximately 90% of all outbreak of viral gastroenteritis. Each year, mortality due to NoV is estimated at 570-800 in the United States, with approximately $777 million in health-care costs. NoV, a genus within the *Caliciviridae* family, is small non-enveloped virus with a positive single-stranded RNA genome of 7.5-7.7 kb organized into three open reading frames (ORFs). ORF1 encodes six non-structural proteins, including RNA dependent RNA polymerase (RdRP). ORF2, ORF3 encode VP1 and VP2 capsid proteins. Generally, the genome of RNA virus has been known to change constantly from mutational event and revealed novel variant. In the previous reports, the NoV GII.4 strains had been known to evolve at a rate of 4.3-9.0X10-4 mutations per site per year and to share a most recent common ancestor in the early 1980s. The goal of this study was to analyze NoV complete sequence and detect variants using next generation sequencing (NGS) method. Sequence reads of NoV were constructed to GII.4 whole genome sequence and were assembled with reference genome. In phylogenetic analysis, the sequence was clustered with 2006b variants. Moreover, VP1 (i.e. capsid protein) were revealed that the amino acid sequence altered three sites in hyper variable domains, and it led to changes in protein structure. Continued molecular studies of NoV by NGS, including approaching of complete genome, is important for monitoring emerging strains in our strategy to prevent of NoV outbreaks in Korea.

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Risk factors for human cutaneous anthrax outbreaks in the hot-spot districts of Northern Tanzania: An unmatched case-control study

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Bacillus anthracis is an aerobic, gram positive and spore forming bacterium, which causes anthrax in herbivores. Humans get infected after coming into contact with infected animals' products. Unmatched case control study was conducted to identify the importance of demographic, biological, and/or behavioural factors associated with human cutaneous anthrax outbreaks in the hot-spot areas of Northern Tanzania. A semi-structured questionnaire was administered to both cases and controls. The age range of participants was from 1-80 years with a median age of 32 years. In the younger group (1-20 years), the odds of being infected were 25 times higher in the exposed group compared to the unexposed group (OR=25, 95%CI=1.5-410). In contrast, the odds of exposure in the old group (≥20 years) were three times lower in the exposed group compared to the unexposed group (OR=3.2, 95% CI=1.28–8:00). Demographic characteristics, sleeping on animal's skins, contact with infected carcasses through skinning, butchering and not having formal education were linked to exposure for anthrax infection. Hence, a one health approach is inevitable for prevention and control of anthrax outbreaks in the hot-spot area of Northern Tanzania.

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Epidemiological characterization of influenza viruses detected from acute respiratory patients in Korea during 2012-2016

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Influenza viruses cause acute respiratory disease, seasonal epidemics and occasional global pandemics. In this study, we investigated the characteristics of influenza virus isolated from patients with acute respiratory illness in Gyeonggi province during 20012/13-2015/16. Influenza viruses were detected in 400 out of 2,726 (14.7%) specimens by using real-time PCR with viral specific primers. Of the positive specimens, 233(58.2%) were identified as A type, and 167(41.8%) were identified as B type. Among the influenza A viruses, 81(20.2%) were classified as subtype A(H1N1)pdm09 and 152(38.0%) were classified as subtype A(H3N2). Depending on the age groups, prevalence was the highest in the school-age and adolescent age group of 7~18 years. Major clinical symptoms were fever(88.0%), cough(83.3%), sputum(69%) and rhinorrhea(68%). While comparing the diseases associated with influenza A and B, there are no district clinical symptoms that would distinguish influenza A from B. These results obtained from the influenza surveillance system could be used as a basis for preparing for the seasonal or pandemic influenza outbreak.

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Cytomegalovirus infection and coronary artery disease: A single center serologic study in north-western Iran

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Background: The role of chronic *cytomegalovirus* (CMV) infection and inflammation in the pathogenesis of atherosclerosis and coronary artery disease (CAD) is still not clear. In this study the aim is to investigate the seroprevalence of anti-CMV antibodies and inflammatory markers in patients who were undergone diagnostic coronary angiography for clinical suspicion of CAD.

Methods: In this cross-sectional descriptive study, 181 patients were selected randomly among those who were referred for diagnostic coronary angiography to the Seyyedoshohada Heart Hospital of Urmia, in the north-western region of Iran (Aug 2012- Dec 2013). Patients were categorized into either of CAD or non-CAD groups, based on their angiography findings. Anti-CMV IgG and IgM antibodies were tested using the enzyme-linked immunosorbent assay (ELISA) method. Serum C-reactive protein (CRP) was measured by a qualitative method (Aniston Kit).

Results: A hundred and forty one patients (77.9%) had atheromatous plaques in their coronary arteries in angiography, and in 40 cases (22.1%), coronary arteries were free of any plaque. Based on the ELISA results, 171 (99.4%), 21 (12.0%), and 112 (62.9%) cases were respectively seropositive for anti-CMV IgG, IgM, and CRP. 99.3% in the CAD group and 100% in the non-CAD group were anti-CMV IgG positive. The rates for anti-CMV IgM seropositivity were 11.7% in CAD group versus 13.2% in non-CAD group, p=0.78. Groups with and without angiographically-documented CAD, had no significant difference in terms of their CRP seropositivity (64.7% vs. 56.4%, p=0.34).

Conclusion: Regardless of having angiographically-proven CAD or not, almost all cases who referred for coronary angiography in our study, had a previous exposure with CMV infection as determined by the presence of anti-CMV IgG antibodies in serum. No association was observed between CMV infection and the presence of CAD, which could be justified with the high rate of CMV-specific IgG antibody seropositivity.

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A Study on the Prevalence of Adverse Ocular Manifestations in Pediatric Patients Receiving Ethambutol in the Revised National Tuberculosis Control Program at East Avenue Medical Center and District II Health Centers in Quezon City

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Tuberculosis is one of the most important systemic infections throughout the world. Ethambutol has been used to treat tuberculosis since the 1960s, but the related visual impairment was recognized soon after its introduction. Objective of the study is to determine the prevalence of adverse ocular manifestations after taking Ethambutol as part of the treatment regimen of children with Tuberculosis. This is a cross – sectional analytical study. Patients aged 3 – 18 years old enrolled for treatment of tuberculosis at the TB DOTS facility of East Avenue Medical Center and District II Health Centers in Quezon City were included in the study. Patients without prior diagnosis of any opthalmologic problems and without history of previous ophthalmologic signs and symptoms were included. Pertinent demographic factors, personal and medical history of patients were obtained. Visual acuity by Snellen chart, color vision by the Ishihara Chart, direct fundoscopic examination, and anterior segment slit-lamp biomicroscopy were performed. Statistical analysis used were Mann Whitney U Test, Yates' chi-square test, Fisher's Exact test, Chi-square test. Statistical significance was based on p-values ≤ 0.05. Results: 93 out of 101 patients had no ocular manifestations, however, 8 (7.9%) of the subjects had ophthalmologic findings; 1 had red-green color vision defect, 6 with error of refraction, and 1 had blurring of superior disc margin in both eyes with red-green color vision defect. There was no significant relationship on the dosage and duration of the drug to the manifestation of optic symptoms of the patients. Study showed that there was no significant ophthalmologic effect on children taking ethambutol provided that the drug will be given within the recommended dose and duration. Patients however, should be monitored for any visual manifestations during treatment.

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Risk factors of multi drug resistant tuberculosis among pediatric patients: A retrospective cohort study

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This study determines the risk factors of pediatric patients diagnosed with multi drug resistant tuberculosis (MDR-TB) conducted in a tertiary hospital in Quezon City and Health Centers from January 2011 to December 2016. A minimum cohort study of 156 patients of 0-18 years old, either bacteriologically confirmed or clinically diagnosed tuberculosis was included in the study. Patients whose significant data of their charts went missing were excluded in the analysis. The following information were gathered a) demographic profile of age, gender, nutritional status, socioeconomic status, district b) clinical profile: history of exposure, results of laboratories, clinical presentation, delay in treatment, previous treatment with tuberculosis and outcome. 162 patients were analyzed, 12/162 had MDR- TB and 150/162 had Non MDR-TB. Results of univariate analysis showed that age and symptoms of weight loss, back pain, night sweats and fever had significant association with MDR-TB, of these factors, back pain (p=0.001; RR:31.771; 95% CI:3.801, 265.554) and fever (p=0.020; RR:7.6587; 95% CI:1.380, 42.494) were independent factors significantly related with MDR-TB. Age, weight loss, back pain, night sweats and fever had significant association with MDR-TB. Larger sample population and a prospective study is recommended to assess the epidemiologic data and further identify other possible risk factors for resistance.

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In vitro and *In vivo* anti-malarial activity of extracts from *Terminalia mantaly* (combretacéae)

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The emergence of resistance of malaria parasite to available drugs highlight the urgent need to develop new efficient, safe and affordable drugs. In Cameroon, medicinal plants such as T. mantaly are used in traditional medicine for the treatment of malaria and have been playing an important role in the fight against malaria especially in rural community. However, their efficacy are still to be validated. This work aimed to investigate the *in vitro* and *in vivo* antimalarial potency of extracts from Terminalia mantaly. Extracts from stem barks, leaves and roots of T. mantaly were macerated in water and methanol. The susceptibility of red blood cells to the extracts was using the MTT assay. The antiplasmodial activity was performed on the W2 strain of Plasmodium falciparum. Prior to the curative test, acute toxicity of the promising aqueous stem bark extract was assessed in mice at a dose of 2,000 mg/kg/bw. Mice infected with P. berghei MRA 406 strain were treated with the promising extract at doses of 100, 200, 400mg/kg. Their parasitemia were monitored as well as their hematological, biochemical and histological parameters. Extracts did not shown any cytotoxicity on erythrocytes at up to 1mg/mL. Out of the six extracts tested, two presented *in vitro* antiplasmodial activity with IC50 of 0.809 and 2.203 µg/ml respectively. The acute toxicity assay of the aqueous extract from stem bark revealed 50% lethal dose (LD50) higher than 2000mg/kg per body weight. The curative test showed an effective dose that reduce 50% of parasitemia (ED50) of 69.50mg/kg with no significant effect on biochemical, hematological and histological parameters. The results from this investigation support the traditional usage of T. mantaly and suggest that stem bark of T. mantaly could be potential source of compounds with anti-malaria activity. However, further investigations are needed to characterize active principles.

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Luetic cervical lymphadenitis in a young adult

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The most effective non-invasive tools for determining the cause of adult cervical lymphadenopathy are fine-needle aspiration and core needle biopsy. If inflammation rather than malignancy is indicated, serologic tests for syphilis should be performed in cases of persistent disease. Syphilis is a sexually transmitted disease by *Treponema pallidum*, and characterized by chancre formation at the site of infection. Regional lymph nodes can be affected, but isolated syphilitic lymphadenitis without chancre is not common. We report a case of syphilitic lymphadenitis with inconspicuous history of syphilis infection. A young adult presented cervical lymphadenopathy without any mucosal disorder in head and neck. Oral antibiotics failed to improve the condition, although core needle biopsy suggested an infectious cause. Serological tests revealed evidence of syphilis infection and excisional biopsy was performed for definite diagnosis. Pathologic review concluded on syphilitic lymphadenitis, which was resolved by benzathine penicillin therapy. Syphilis should be considered as a cause of cervical lymphadenopathy in adults.

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Biological diversity of avian influenza viruses in birds circulating in the Asian part of Russia

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The disease of animals and humans, called influenza, is caused by representatives of the family of Orthomyxoviruses. The waterfowl and shorebirds are supposed to be a natural reservoir of the most subtypes of AIV. The territory of Western Siberia is located in the center of Eurasia and is intersected by three main bird migratory routes, pathways from Europe, Africa, Asia and Oceania. The study of the biological diversity of AIV in wild birds at the territory of Western Siberia was carried out in 2007-2018. 3,375 samples were collected from birds of 8 orders. 285 strains of AIV (including HPIV) were isolated from the material, collected from Anseriformes. During the period from 2007 to 2018, the percentage of viruses in the Anseriformes varied from 5.6% to 20%. The order of the Charadriiformes is characterized by lower percentage of virus isolation. In our study, the percentage of AIV isolation from this species was 1.4%. Phylogenetic analysis of the M gene of all isolated AIV strains showed that they belong to the classical avian-like viruses. All viruses on the phylogenetic tree of the M gene are located chaotically, which indicates the persistence of various variants of the M gene in the wild bird population of Western Siberia. Thus, Western Siberia plays an important role in the persistence of avian influenza viruses, their evolution and geographical distribution in the Eastern Hemisphere.

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Sepsis associations with HLA-DR and -DQ genes

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Aim: Despite the extended laboratory and clinical study of sepsis, its diagnosis remains a clinical challenge. The initiation of sepsis activates many different biochemical and immunological pathways, which is expressed with alterations of many molecules on human tissues. The aim of this research was to investigate the genetically determined predisposition to developed sepsis by analysis of distribution of human leukocyte antigen HLA class II genes. We summarize the evidence for a genetic susceptibility to develop the sepsis and unfavorable outcome of sepsis. We consider the candidate genes are likely to be involved in the pathogenesis of sepsis and based on genetic variability.

Method: This was a single-center study at Pauls Stradins Clinical University Hospital in Latvia. The study group consisted of patients (n=62) who had sepsis who were enrolled during an 8-month period. The immunogenetic part of the study was done and 62 sepsis patient and control group, samples of 100 healthy individuals who were genotyped for HLA-DRB1; DQB1 and DQA1 using RT-PCR with sequence-specific primers.

Results: Summarized results shows that the alleles: DRB1*04:01 (OR=5.54; 95%CI=1.88-16.29; p=0.001); DRB1*07:01 (OR=19.03; 95%CI=2.37-152.82; p=0.001); DQA1*05:01 (OR=14.17; 95%CI=5.67-35.4; p<0.001); DQB1*02:01 (OR=50.00; 95%CI=2.90-861.81; p<0.001) were significantly increased in patients with sepsis compared to the control group patients. Comparing these alleles who were significantly increased in patients with sepsis compared to the control group patients with the most common final clinical diagnosis was pneumonia 66% (n=41).

Conclusion: Undoubtedly, our preliminary data shows that development of sepsis can have association with opedelenny alleles of genes HLA class II. These results have to be confirmed prospectively in a large population.

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Preclinical multimodel imaging of bacterial infections and the potential for clinical translation

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Each year more than 70 billion standard units of antibiotic are prescribed to treat bacterial infections worldwide. In addition, at least 63,000 tons of antibiotics are consumed by livestock for growth promotion and disease prevention. The result of this overuse of antibiotics is a spiraling increase in resistance. In the United States and Europe, antibiotic resistant bacteria are responsible for more than 4 million infections and approximately 50,000 deaths annually. In addition, bacteria such as methicillin-resistant Staphylococcus aureus (MRSA) have increased in prevalence in hospitals over the last three decades. Such bacteria are particularly problematic in postoperative infections, exacerbating treatment through the development of biofilms, especially on medical implants which are extremely hard to treat without removal and replacement of the device. This presentation will show how non-invasive preclinical imaging (optical, PET and CT) is being used to better understand the establishment and development of bacterial infections in a number of defined animal disease models of bacterial infections, and how best to treat them. In particular, data will be shown as to how preclinical imaging can be used to monitor biofilms on orthopedic implants and how this technology might be translated into the clinic.

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Predictors used to assess virological response to direct acting anti-HCV therapy

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Hepatitis C is an infectious disease affecting primarily the liver, caused by the hepatitis C virus (HCV). HCV infection is a major problem in Egypt. Egypt has the highest prevalence of the Hepatitis C virus (HCV) in the world, with 14 percent of the population infected and 11.8 million patients, according to the World Health Organization. Every year there are 170,000-200,000 new HCV cases in Egypt. It was first discovered in 1989. HCV is a small, enveloped, single-stranded, positive-sense RNA virus. It is a member of the Hepacivirus genus in the family *Flaviviridae*. There are seven major genotypes of HCV, which are known as genotypes one to seven . It is transmitted by injection which means spread primarily by blood-to-blood contact associated with intravenous drug use, poorly-sterilized medical equipment, and transfusions. Aim of the study: This study aims to determine the common prevalent HCV genotypes among chronic HCV patients in Egypt and to evaluate the rate of sustained virological response (SVR) with some factors that affecting it. Subject & Methods: In our study fifty patients were enrolled. Eligible participants were aged ≥18 years, had chronic HCV genotype 4 infection (serum HCV RNA≥2000 IU/mL). All Biochemical tests for liver function, Blood sugar and HBA1C were done for all cases. The recommended regimen was DCV 60 mg plus SOF 400 mg once daily for 12 weeks; at their discretion, physicians could add RBV to the regimen or reduce treatment duration. HCV-RNA (viral load) was measured using RT-PCR (quantitative method) (Qiagen/BD Company) (Before treatment & After 12 weeks) and serum Neopterin ELISA kit. Results: SVR achieved 12 weeks after the end of treatment. Of the 50 evaluable patients, 6 received DCV+SOF and 44 DCV+SOF+RBV. Most patients were men (76%). SVR12 (modified intention-to-treat) was achieved by 98% of patients (48/50); 1 patient had virological breakthrough (was lost to follow-up at 4 weeks after treatment) and 1 patient was Non-responder. There was no statistically significant difference in treatment efficacy between treatment-naive patients (100%, 37 of 37) and those with treatment experience (84.6%; 11 of 13) (P=.51). High SVR12 was observed regardless cirrhosis. There was a reduction in the mean neopterin level in patients after treatment in comparison to pre-treatment level; however this reduction didn't reach a statistical significant value. Conclusions: In our study, the most predominant genotype was genotype IV with 86%. Of our HCV-treated patients, had high SVR. HCV genotype-4, and low baseline viral load were predictive of SVR.

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3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGR) from *Leishmania* donovani is indispensible for the parasites as depicted by gene knockdown studies

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*Leishmania*sis is one of the most diverse and complex of all vector borne diseases which are transmitted through the bite of infected female Phlebotomine sand flies. Existing anti*leishmania*l drugs are associated with toxicity, resistance issue, high prices and lack of quality during administration and long treatment length. Sterols are the important components of the cell membrane which are essential for cellular functions and maintain the cell structure. In humans, HMGR is a rate limiting enzyme of cholesterol biosynthesis and is a trans-membrane glycoprotein. In *Leishmania*, however HMGR exists as a soluble protein involved in ergosterol biosynthesis. The sterol biosynthetic pathway in *Leishmania* is considered to be an important drug target. In the present study, null mutants of LdHMGR were generated by homologous recombination and mutants were confirmed by PCR, western blotting and enzyme activity. The ergosterol level was quantified by HPLC method and found that the SKO LdHMGR parasite ergosterol level was low when compared to WT parasite and 99.14% reduction was observed in DKO LdHMGR. Growth curve analysis of SKO LdHMGR was found to be less with rapid reduction in growth rate of the DKO LdHMGR promastigotes as compared with WT promastigotes. Infectivity analyses showed decreased percentage of host cell line infection by null mutants of LdHMGR as compared to SKO LdHMGR and WT promastigote parasite. This data suggests that HMGR plays an essential role in growth and infectivity of parasite and it is an essential enzyme and can be utilized for future anti*leishmania*l chemotherapeutic intervention.

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