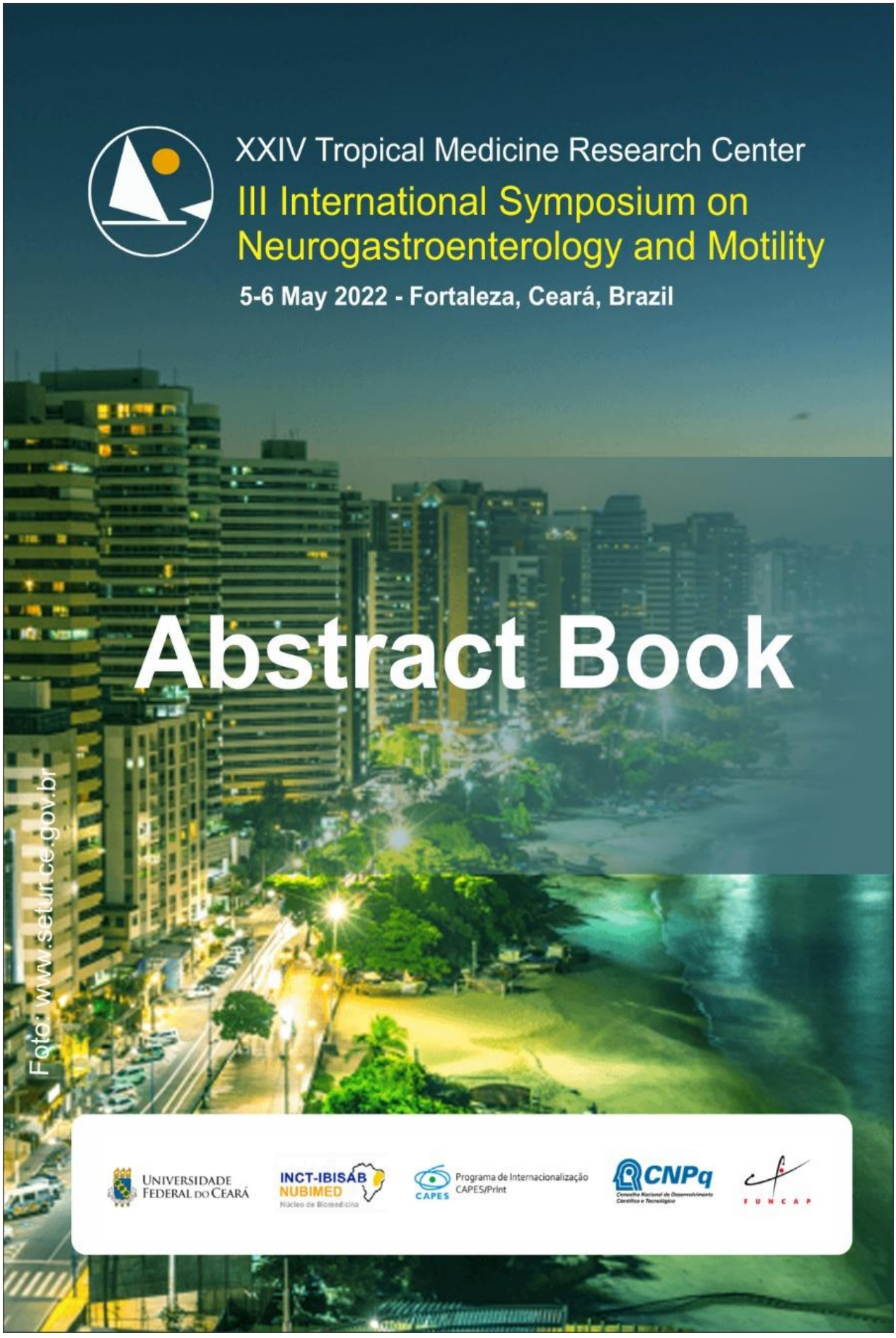
XXIV Tropical Medicine Research Center

III International Symposium on Neurogastroenterology and Motility

5-6 May 2022 - Fortaleza, Ceará, Brazil

Abstract Book



Universidade Federal do Ceará

INCT-IBISAB NUBIMED Núcleo de Biomedicina

CAPES Programa de Internacionalização CAPES/PrInt

CNPq Conselho Nacional de Desenvolvimento Científico e Tecnológico

FUNCAP

XXIV Tropical Medicine Research Center

&

III International Symposium on Neurogastroenterology and Motility

CAPES Print International Program in Biomedicine

Biomedicine Center, Faculty of Medicine
Federal University of Ceara

5-6 May 2022

Fortaleza, Ceará, Brazil

[1] ***Communication address to***: Cel. Nunes de Melo St, 1315, Rodolfo Teófilo, Fortaleza, CEP 60.430-270, CE, Brazil. **E-mails**: alima@ufc.br; adm-upc@ufc.br; filhonego@yahoo.com.br; **Phones**: 55-85-3366-8445 or -8437; **Cel.**: 55-85-98704-2833.

Introduction

The annual meeting in Tropical Medicine and Hygiene & Pharmacology is a regular scientific event, which started in 1996 and now complete its twenty-fourth edition. The event was created to bring together professors, researchers, and students interested in the scientific and technological development of research on tropical diseases that afflict populations in the Brazilian semiarid region. Initially the event was held by effective participation of three national and three international researchers' groups. The Brazilian groups were led by professors Aldo AM Lima, Federal University of Ceara, Edgar M. Carvalho, Federal University of Bahia, and Selma Jerônimo, Federal University of Rio Grande do Norte. The international groups were led by the researchers, Richard L. Guerrant, University of Virginia, CHO, VA, Warren Johnson, Cornell University, NY, and Lee W. Riley, University of California, Berkeley, CA. The event has covered topics of ongoing research and perspectives in several areas of tropical medicine such as leishmaniasis, leptospirosis, diarrheal diseases, tropical enteropathy, malnutrition, human T-lymphotropic virus (HTLV), human immunodeficiency virus (HIV), leprosy, tuberculosis, among others. The event will be held in Fortaleza, CE, May 5-6, 2020. It is open to the public of researchers, professors, undergraduate and graduate students, as well as technical personnel, receiving annually 40-60 people. The event has contributed to the development of research in tropical medicine and hygiene & pharmacology, sustaining research networks at the regional, national and international levels in areas of interest in public health, especially in the Brazilian semiarid region. In the last seven years, we have the effective participation of two INCTs (Biomedicine- http://www.nubimed.ufc.br and Immunology of Tropical Diseases-inct.cnpq.br/web/inct-dt). The event has been fundamental in the creation of a long-term sustainable research networks (RECODISA: http://www.recodisa.ufc.br; MAL-ED: http://www.upcibimed.ufc.br/MAL-ED) as well as to revigorated the postgraduate degrees in Medical Sciences (Level 6 CAPES), Microbiology (Level 5 CAPES), Pharmacology (Level 6 CAPES) and Morphofunctional Sciences (Level 4 CAPES), as well as demonstrating its importance in national and global public health.

Figure 1 - Photo of the speakers and students' participants of the II Annual Meeting of the Tropical Medicine Research Center in Salvador, BA, March-1997.

Brief history of previous editions

In the last forty years, initially two national research groups, led by professors Aldo AM Lima and Edgar M. Carvalho, developed important lines of research related to tropical medicine, leishmaniasis and diarrheal diseases & malnutrition, at Universidade Federal do Ceará and Bahia, respectively. Subsequently, a third group led by Professor Selma Jerônimo from the Federal University of Rio Grande do Norte, also emerged in the in leishmaniasis theme. From the beginning, these three research groups have maintained relevant and significant international collaboration with international groups led by researchers, Richard L. Guerrant, Warren Johnson, and Lee W. Riley. The development and progress of these research groups led to the aggregation of new researchers and financial support by national research funding agencies, CNPq and CAPES, as well from abroad, such as the National Institute of Health (NIH), Bethesda, MD, and most recently the Bill and Melinda Gates Foundation. The common environment of research related to tropical medicine led to the formatting of the event, Annual Meeting in Tropical Medicine Research Center & Pharmacology. The first meeting took place in mid-March 1996. **Figure 1** illustrates only the researchers participating in the II Annual Meeting of the Tropical Medicine Research Center in Salvador, BA, in March-1997. Note researchers Lee W. Riley (1st from left to right), Aldo AM Lima (3rd), Edgar M Carvalho (6th in the first line), Selma Jerônimo (8th in the first line), Richard Pearson, UVa, CHO, VA (1st. On the second line), and Warren Johnson (2nd. On the second line).

Figure 2 shows the team of speakers, graduate and undergraduate students which attended the XXIII Tropical Medicine Research Center in December 2019. The longevity of this event is based mainly on the regional, national and international interaction and collaboration of researchers interested with lines of research on Tropical Medicine and Hygiene & Pharmacology. This network has engedered a fruitful scientific and technological production, allowing the training of human resources at postgraduate, graduate, and technical level. Over this period were developed two international research agreements between UFBA & University of Cornell and UFC, UFRGN & University of Virginia, which today constitute international scientific and technological cooperation models for several other national and international institutions. As a result of the promotion of these annual and regular meetings, it was developed two INCTs, Biomedicine and Immunology of Tropical Diseases, and two research networks, RECODISA (www.recodisa.ufc.br) and MAL-ED (www.mal-ed.fnih.org), nationally and internationally. The list of participants in these events and today formed through national and international graduate programs as evidenced in the leaders' CVs lattes, demonstrates the training capacity of human resources that had directly or indirectly promoted these annual and regular meetings of the Tropical Medicine Research Center. Leading researchers were recognized by national and international societies such as the Brazilian Society of Tropical Medicine, the American Society of Tropical Medicine and Hygiene, ASTMH and the Brazilian Academy of Sciences, ABC. The quality of this training can be realized by the fact that the majority, > 80% of graduates, are now researchers and / or professors from national and / or international institutions. It is important to mention that these international collaborations has been essential for the international insertion of our graduate programs. The quality of this academic exchange was recognized by the CAPES, principal Brazilian agency dedicated for the Improvement of Higher Education Personnel, which aproved the project “Internationalization of the Federal University of Ceará in Translational and Epidemiological Research in NeuroGastroenterology”, according the therms of the International Collaboration Program CAPES-PRINT (2018-2022), recently renowned for the next three years. By the way, it allowed to expand the academic exchange of the Federal University of Ceará to the *Queen Mary University of London* with Prof. Daniel Sifrim, a world-renowned expert on esophageal motility, as well as to the University of Liverpool with Prof. David Criddle, a lecturer on molecular physiology & cell signaling with long-standing interest on calcium and ROS roles in acute pancreatitis.

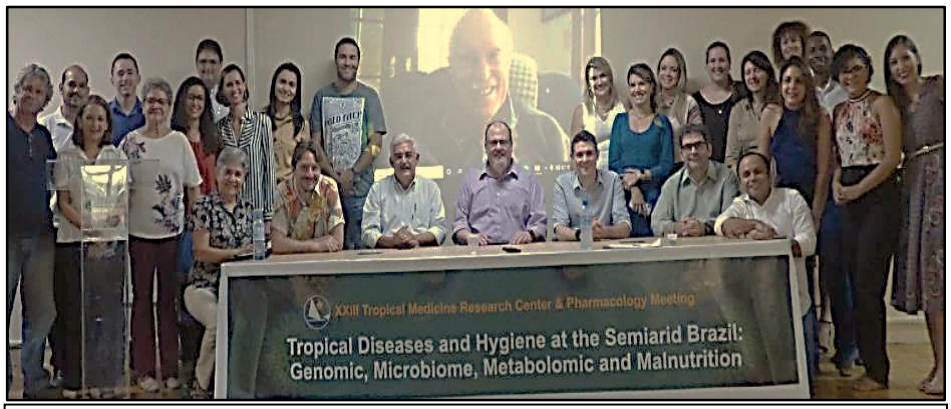


Figure 2 - Photo of the speakers and students participating at the XXIII Annual Meeting of the Centro de Medicina Tropical in Fortaleza, CE, December 2019. Dr. Guerrant on the online projector image and sited on the table from left to right: Prof(a)s Selma, Alexandre, David, Jonathan, Reinaldo, and Dr. Vinicius.

Due to the Covid-19 pandemic, the event was interrupted. In 2022, the XXIV Tropical Medicine Research Center & Pharmacology and III International Symposium in Neurogastroenterology and Motility will be resumed, this time via Internet, allowing a broader attendance. As one can see in the preliminary program, the event is structured as usual, i.e. with sessions dedicated to major public health problems, with lecture by scholars and oral presentations by graduate students followed by discussion with the audience.

XXIV Tropical Medicine Research Center

PROGRAM

Thursday – 5 Mayth

8:30 - 9:00 am	***Opening remarks***: ***José Cândido Lustosa Bittencourt de Albuquerque*** Rector, Federal University of Ceara **José Glauco Lobo Filho** Vice-Rector, Federal University of Ceara ***Francisco Rodrigo Porto Cavalcanti*** Pro-Rector Researcher and Postgraduation, Federal University of Ceara ***João Macedo Coelho Filho*** Director, Faculty of Medicine, Federal University of Ceara ***Tarcísio Haroldo Calvacante Pequeno*** Presidente da Funcap-CE ***Aldo Ângelo Moreira Lima*** Coordinator, XXIV TMRC & Pharmacology Meeting and Center of Biomedicine, Faculty of Medicine, Federal University of Ceara ***Armênio Aguiar dos Santos*** Coordinator, III International Symposium in Neurogastroenterology and Motility Center of Biomedicine, Faculty of Medicine, Federal University of Ceara

XXIV Tropical Medicine Research Center
III International Symposium on Neurogastroenterology and Motility

Capes Print International Program in Biomedicine, NUBIMED, FAMED, UFC
5-6 May 2022 – Fortaleza, Ceará, Brazil

Session I: Environmental enteric dysfunction, enteric infections, and malnutrition.

Chairpersons*: Profs. Aldo AM Lima / Alexandre Havt*

9:00 - 9:25	**Measuring lactulose and mannitol levels to assess environmental enteric dysfunction and malnutrition in children** Lyvia MVC Magalhães, Federal University of Ceara
9:25 - 9:50	**Calcium-binding protein Inhibitor attenuates intestinal damage and diarrhea severity during *Clostridioides difficile* Infection by modulating inflammatory response** Deiziane Viana da Silva Costa, University of Virginia & Federal University of Ceara
9:50 - 10:15	**Consumption of a multi-deficient diet causes dynamic changes in the intestinal morphofunctional barrier, body composition and impaired physical development in post-weaning mice** Samilly SA Ribeiro, Federal University of Ceara & Federal University of RGN & University of Virginia
10:15 – 10:40	***Break***
10:40 - 11:05	**Impact of subclinical enteroaggregative *Escherichia coli* infection and coinfections on the gastrointestinal epithelial barrier and child growth: a multi-center cohort study** Virginia LSC Urtiga, Federal University of Ceara

Lunch Break

Session II: Nutrition and Metabolomics applied to environmental enteric dysfunction, enteric infections, and malnutrition.

Chairpersons: *Profs.* Jonathan Swann / Sean R Moore

13:30 - 13:55	**Environmental enteric dysfunction, enteric infections, and malnutrition: a role for metagenomic studies** Aldo AM Lima, Federal University of Ceara
13:55 -14:20	**Redefining enteroaggregative *Escherichia coli*: a genomic new prospective** Alexandre Havt, Universidade Federal do Ceará
14:20 -14:45	**Bile acid profiling reveals distinct signatures in undernourished children with environmental enteric dysfunction** Sean R. Moore, University of Virginia, Charlottesville, VA, USA
14-45 -15:10	**Characterizing the biochemical alterations associated with environmental enteric dysfunction using metabolomics** Jonathan Swann, University of Southampton, UK
15:10 – 15:45	**Modeling enteropathy or diarrhea with the top bacterial and protozoal pathogens: update on differential determinants of outcomes** Richard L. Guerrant, University of Virginia, Charlottesville, VA, USA

Break

Session III: Leishmaniasis a common endemic disease: epidemiology, clinical, immunology and genome.

Chairpersons: *Profs. Anastácio de Queiroz Sousa* / Selma Jerônimo

16:00 -16:25	**Leishmaniasis in the semiarid area of Brazil: clinical and epidemiology** Anastácio de Queiroz Sousa, Federal University of Ceara
16:25 - 16:50	**Leishmaniasis and coinfections in dogs in the urban community of Fortaleza, Ceará, Brazil** Adam L Lima, Ph.D., Abbott Laboratories and State University of Ceara
16:50 - 17:15	**Role of immune-inflammatory biomarkers and pathobiology in leishmaniasis** Selma Jerônimo, Federal University of Rio Grande do Norte
17:15 – 17:40	**Colorimetric and fluorometric LAMP for species-specific detection of *Leishmania* spp.** Rubens Lima do Monte Neto, FIOCRUZ, MG

XXIV Tropical Medicine Research Center

Friday – May 6th

Session IV: SARS-CoV-2 and Influenza A/B virus in human and animal studies

Chairpersons: Profs. Eurico Arruda / Roberto J Pires Neto

8:35 – 9:00	**A brief look at coronavirus pathogenesis** Eurico Arruda, State Univesity of São Paulo, Ribeirão Preto, SP
9:00 - 9:25	***SARS-CoV-2* pathobiology in mild and moderate acute human respiratory infection** Rafhaella Gondim, Federal University of Ceara
9:25- 9:50	**N-acetylcysteine: molecular mechanisms of cell preservation against inflammatory aggression of SARS-CoV-2 infection** Hugo Pequeno Monteiro, Escola Paulista de Medicina, UNIFESP, São Paulo, SP
9:50-10:15	**Clinical, control, double-blind, randomized trial with N-acetylcysteine and bromhexine for COVID-19: preliminary results** Roberto J Pires Neto, Federal University of Ceara
10:15-10:40	**Intestinal epithelial barrier function and SARS-CoV-2 spike glycoprotein: function and pathobiology using Ussing Chamber model in murine** José Kleybson Sousa, Federal University of Ceara
10:40-11:05	***SARS-CoV-2* spike glycoprotein triggers intestinal chloride hypersecretion and inflammation in murine model** Cristhyane Costa de Aquino, Federal University of Ceara
11:05-11:30	**Detection of SARS-CoV-2 in different human biofluids using the loop-mediated isothermal amplification assay: a prospective diagnostic study in Fortaleza, Brazil** Marco Clementino, Federal University of Ceara
11:30-11:55	**Avian influenza: the new paradigm of H_5 viruses** Helena Lage Ferreira, Faculdade de Zootecnia e Engenharia de Alimentos da USP - FZEA/USP, SP, Brasil
11:55 – 12:20	**Influenza in pregnancy and childbirth in the Brazilian semiarid: the INFLUEN-SA study** José Quirino Filho, Federal University of Ceara

III International Symposium on Neurogastroenterology and Motility

Friday – May 6th

Session V: Neurogastroenterology and motility diseases: nonerosive reflux disease, inflammation, mucosal integrity, and pancreatitis

Chairpersons: *Profs. Marcellus P Souza / Armenio A Santos*, Federal University of Ceara

13:30 - 13:55	**Gastro-esophageal reflux disease: News in pathophysiology and diagnosis** Daniel Sifrim, Queen Mary University of London, UK
13:55 -14:20	**Distal esophageal exposure is associated with inspiratory oral pressure, a measurement of the diaphragm strength, particularly in aging** Miguel Ângelo Nobre e Souza, Universidade Federal do Ceara
14:20 -14:45	**The role of Ca^{2+} signaling in the physiology and pathophysiology of exocrine pancreas** David Criddle, University of Liverpool, UK
14-45 -15:00	**Impact of the physical exercise on the gastrointestinal dysmotility** Moisés Tolentino Bento da Silva, Universidade do Porto, Portugal
15:00 – 15:15	**Activation of the ubiquitin-proteasome pathway in the crural diaphragm in reflux esophagitis** Suliana Mesquita Paula, Universidade Federal do Ceará
15:15 – 15:40	**Role of bile acids in the contractile activity of rat esophageal segments** Kaline Kelly Lima Gadelha, Universidade Federal do Ceará

Scientific Committee:

[1] Aldo AM Lima, M.D., Ph.D., Federal University of Ceara

Alexandre Havt, Ph.D., Federal University of Ceara

Armênio A Santos, M.D., Ph.D., Federal University of Ceara

Marcellus HLP Souza, M.D., Ph.D., Federal University of Ceara

Pedro JC Magalhães, Ph.D., Federal University of Ceara

9:00 - 9:25	**Measuring lactulose and mannitol levels to assess environmental enteric dysfunction and malnutrition in children** Lyvia MVC Magalhães, Federal University of Ceara

Lyvia M. V. C. Magalhães, Francisco A. P. Rodrigues, José Quirino-Filho, Rafhaella N.D.G. Gondim, Samilly Ribeiro, José K. Sousa, Marco Clementino, Bruna L.L. Maciel, Alexandre Havt, Armênio A. Santos, Pedro J.C. Magalhães, Aldo A.M. Lima.

Environmental enteric dysfunction (EED) and malnutrition are prevalent in poor populations and predispose to short stature and deficits in children's neurocognitive development. Objectives: We describe here high performance liquid chromatography (HPLC) coupled with tandem mass spectrometry (MS/MS) as a method to assess the functional gastrointestinal barrier (FGB) in children. Material and Methods: Liquid chromatography coupled to a Q-TRAP 5500 mass spectrometer was used to measure lactulose and mannitol compounds. FGB was evaluated by the lactulose:mannitol (L:M) ratio obtained from urine samples from 76 children belonging to three experimental groups: (a) healthy control group (C=18) and economic class group with a high human development index (HDI = 0.90); (b) children with EED (28) and low HDI economic class (0.21); and (c) DN children (30) with similarly low HDI and weight-for-age z-score <-2. Results: The accuracy in the measurement of lactulose and mannitol was demonstrated by the recovery at three concentration levels (100, 500 and 1000 ng/mL) and in triplicate, with recovery values above the recommended. Intermediate precision was determined at 24h intervals and coefficients of variation were less than 8.7%. The L:M ratio was shown to be altered in the EED and malnutrition groups compared to the C group. The mannitol excretion rate was shown to be reduced in the EED and malnutrition groups compared to the C group. Conclusions: The determination of the L: ratio M by HPLC-MS/MS has sensitivity, specificity and accuracy to document changes in FGB, mainly in the reduction of the absorption area, in children with different HDI and risk for EED and malnutrition. The method is useful for assessing the risk of environmental and frequent subclinical enteric infections associated with EED and malnutrition.

Key words: Functional gastrointestinal barrier, environmental enteric dysfunction, malnutrition, HPLC-MS/MS.

9:25 - 9:50	**Calcium-binding protein Inhibitor attenuates intestinal damage and diarrhea severity during *Clostridioides difficile* Infection by modulating inflammatory response** Deiziane Viana da Silva Costa, University of Virginia & Federal University of Ceara

9:50 - 10:15	**Consumption of a multi-deficient diet causes dynamic changes in the intestinal morphofunctional barrier, body composition and impaired physical development in post-weaning mice** Samilly SA Ribeiro, Federal University of Ceara & Federal University of RGN & University of Virginia

S. A. Ribeiro[1]; F. A. P. Rodrigues[1]; M. A. Clementino[1]; H. N. Veras[1]; R.C.L. Siqueira[1]; P. H. Q. de Medeiros[1]; J. M. Pereira[1]; M.F.A. Guanabara Júnior[1]; J. K. de Sousa[1]; A.K.S. dos Santos[1]; A.A. dos Santos[1]; B.L.L. Maciel[2]; A. Havt[1]; A. A. M. Lima[1].

[1] Pharmacology Postgraduation Program, Department of Physiology and Pharmacology, Faculty of Medicine, Federal University of Ceará

[2] Nutrition Postgraduation Program and Department of Nutrition, Federal University of Rio Grande do Norte, Natal, Brazil

Abstract

Few studies have focused on nutrient-deficient diets and associated pathobiological dynamics of body composition and intestinal barrier function. This study evaluated the impact of a nutrient-deficient diet on physical development and intestinal morphofunctional barrier in mice. C57BL/6 (21 days of age) mice were fed a Northeastern Brazil regional basic diet (RBD) or a control diet for 21 days. The animals were subjected to bioimpedance analysis, lactulose test, morphometric analysis, and qRT-PCR to evaluate tight junctions and intestinal transporters. RBD feeding significantly reduced weight ($p < 0.05$) from day 5, weight gain from day 3, and tail length from day 14. The intake of RBD reduced total body water, extracellular fluid, fat mass, and fat-free mass from day 7 ($p < 0.05$). RBD induced changes in the jejunum, with an increase in the villus/crypt ratio on day 7, followed by reduction on days 14 and 21 ($p < 0.05$). Percent excretion of lactulose and mannitol decreased in the malnourished group on days 7 and 14, while the lactulose/mannitol ratio increased on day 14 ($p < 0.05$). Changes in intestinal barrier function on day 14 were associated with reductions in claudin-1 and occludin, and on day 21, there was a reduction in the levels of claudin-2 and occludin. SGLT-1 levels decreased on day 21. RBD compromises body composition and physical development with dynamic changes in intestinal barrier morphofunctional. RBD is associated with damage to intestinal permeability, reduced levels of claudin-1 and occludin transcripts, and return of bowel function in a chronic period.

Keywords: Malnutrition; Northeastern Brazil regional basic diet; intestinal barrier function; body composition; tight junction proteins.

10:40 - 11:05	**Impact of subclinical enteroaggregative *Escherichia coli* infection and coinfections on the gastrointestinal epithelial barrier and child growth: a multi-center cohort study** Virginia LSC Urtiga, Federal University of Ceara

OBJECTIVE: To assess risk factors, gastrointestinal barrier integrity, inflammation and innate immune response associated with Enteroaggregative *Escherichia coli* (EAEC) alone or in combination with other enteric pathogens using molecular diagnostics (TaqMan array) and its impact on infant growth at 6 months of age at 8 sites study of a child cohort. **MATERIAL AND METHODS:** A case-control study nested from the multicenter cohort study (MAL-ED network) was performed. To assess isolated EAEC infection and co-detection, the cohort was organized into 7 groups. The main outcome variables were delta Z-scores: length for age, weight for age, weight for length; as a secondary outcome, markers were included to assess the functional gastrointestinal barrier, inflammation and innate immune response in the first 6 months of age among the study groups. **RESULTS:** The mother's lower education, income, as well as inadequate hygiene and sanitation, in addition to a higher proportion of days of antibiotic use were associated with Infections caused by EAEC and 3 or more co-pathogens ($p<0.001$). Intestinal function measured by lactulose/mannitol urinary excretion rate was altered, driven by z scores adjusted for percentages of lactulose excreted in urine, being significantly higher between groups: EAEC with 3 or more pathogens and 3 or more pathogens without EAEC both compared with group 1 and 2 pathogens without EAEC ($p=0,022$; $p=0,043$). Greater inflammation through myeloperoxidase can be seen in the EAEC group with 3 or more pathogens ($p<0,001$). Subclinical infection in the EAEC group with 3 or more co-pathogens influenced lower growth deficits as evidenced by the length-for-age Z-score ($p=0,004$). **CONCLUSION:** This analysis points out that more severe damage to the functional gastrointestinal barrier and subsequent reduction in infant growth are associated with environmental enteric dysfunction, and are often associated with the presence of EAEC combined with other enteropathogens in this infant population studied.

Keywords: Enteroaggregative Escherichia coli. Pathobiology. Epidemiology. Subclinical infections of enteroaggregative E. coli. Environmental enteric dysfunction. Functional gastrointestinal barrier.

13:30 - 13:55	**Environmental enteric dysfunction, enteric infections, and malnutrition: a role for metagenomic studies** Aldo AM Lima, Federal University of Ceara

Aldo AM Lima[1,2], Lyvia MVC Magalhães[1], Francisco AP Rodrigues[3], José Quirino-Filho[1], Bruna LL Maciel[4], Marco Clementino[1], Alexandre Havt[1], Richard L Guerrant[1,2] and MAL-ED Net Work Collaborators.

[1]Federal University of Ceará, Fortaleza, Ceará, Brazil; [2]University of Virginia, Virginia, USA; [3]Federal Institute of Education, Science and Technology of Ceará, Fortaleza, Ceará, Brazil; [4]Federal University of Rio Grande do Norte, Natal, Rio Grande do Norte, Brazil.

Background: Environmental Enteric Dysfunction (EED), Enteric Infections (EI) and Malnutrition (MN) are associated with deficits in child growth and neurocognitive development, in addition to increased morbidity and increased risk of death resulting from the vicious cycle associated with child malnutrition. This study aims to determine the association of microorganisms with EED, EI and MN and the importance of the perspective of a metagenomic approach for the simultaneous diagnosis of microorganisms with application in public health. **Methods:** We used quantitative PCR to detect 29 enteropathogens in diarrheal and non-diarrheal stools collected from children in the first 2 years of life obtained from the international multicenter cohort study called Malnutrition – Enteric Diseases (MAL-ED). The children's compliance was monthly until 12 months of age. We estimated associations between specific etiologic pathogens of diarrhea and subclinical infection by month-length in children at 3, 2, and 5-year longitudinal age intervals, and we estimated a longitudinal age model to account for temporality and time-dependent confounding. Intestinal epithelial barrier function was performed using the lactulose:mannitol test and urine samples from 76 healthy control groups with a high Human Development Index (HDI) of mean 0.90 (N = 18); (b) children with EED and low HDI of mean 0.21 (N = 28); and (c) MN children with similarly low HDI and weight-for-age z-score <−2 (N = 30) from a genetically similar population in a poor region in Northeast Brazil. LC-MS/MS was used to measure lactulose and mannitol levels. To compare the microbiota of malnourished children in the multicenter MAL-ED study with healthy children, we used a temporal conservation of covariance between bacterial taxa in the microbiota of healthy members of a Bangladeshi group in a birth cohort with samples of children aged 1 to 60 months old. Variable region 4 (V4) sequencing of bacterial 16S rRNA genes present in fecal samples were used to determine taxonomic units with ≥97% identical nucleotide sequence for determination of microorganisms in the microbiota of these children. **Results:** We analyzed 6,625 diarrheal stools and 30,968 non-diarrheal surveillance stools from 1,715 children. Viral diarrhea (36.4% of overall incidence, 95% CI 33·6–39·5) was more common than bacterial (25·0%, 23·4–28·4) and parasitic (3·5%, 3·0–5·2). Ten pathogens were responsible for 95.7% of attributable diarrhea in decreasing order of importance: Shigella, sapovirus, rotavirus, adenovirus 40/41, enterotoxigenic *Escherichia coli*, norovirus, astrovirus, *Campylobacter jejuni* or *C. coli*, Cryptosporidium and typical enteropathogenic *E coli*. Substantial decreases in length at 2 years were associated with subclinical, non-diarrheal infection with Shigella (length-for-age Z-score reduction [LAZ] -0.14, 95% CI -0.27 to -0.01), *Escherichia coli* (–0.21, –0.37 to –0.05), Campylobacter (–0.17, –0.32 to –0.01), and Giardia (–0.17, –0.30 to –0.05). Increased enteroaggregative *E coli* co-infection of pathogens in subclinical infections were negatively associated with weight-to-length delta and weight-for-age z-scores in children 0 to 6 months old. Significant reduction in absorption area was mainly observed in children with EED and MN compared to healthy controls. The results of the gut microbiota study revealed an “ecogroup” of 15 covariate bacterial taxa that provide a concise description of the developing microbiota in healthy children in this and other low-income countries, and a means for tracking community redress in treated malnourished children with therapeutic foods. **Conclusions:** These results demonstrate a multiple presence of microorganisms associated with EED, EI and MN in children with a consequent deficit in physical development. The data also demonstrate the importance of new cohort studies with a metagenomic approach for the simultaneous diagnosis of these microorganisms with application in public health.

13:55 -14:20	**Redefining enteroaggregative *Escherichia coli*: a genomic new prospective** Alexandre Havt, Universidade Federal do Ceará

Enteroaggregative *E. coli* (EAEC) has been identified as a bacterium that can cause diarrhea in children and adults living in developed and developing countries. Many studies have described EAEC's genetic heterogenous feature, but unlike other *E. coli* pathotype, EAEC stands alone engaging a phenotypic, rather than genotypic definition. Up to now EAEC has been genetically diagnosed by the presence of the chromosomal gene *aaiC* and the plasmidial gene *aatA*. In addition, many studies have been also classified them as typical or atypical EAEC by the presence of the transcriptional activator encoded by the gene AggR. In this work the authors applied methods of comparative whole genomic sequence on a collection of 97 EAEC strains which were isolated by a multicenter case-control study called GEMS that was sited in countries of Africa and Asia. Approximately 70% of the studied strains harbored at least one of the genes encoding the five known aggregative adherence fimbriae (AFF). However, the ones that lacked an identifiable AFF did not show a complete set of *AggR* regulon. In addition, they also verified strains harboring and ETEC colonization factor (CF22) that showed similar protein structure of an usher-chaperon-pilin family of adhesins that could also adhere to colonoid monolayers like the prototype EAEC strain 042. Among all detected genes this work identified that the genes *sepA*, *iss* and *ompT* were associated with diarrhea cases, but the EAEC strains also showed several genes characteristically found in other *E. coli.* Pathotypes. In conclusion, this work brought a new molecular definition of EAEC, which should comprise *E. coli* strains harboring *AggR* and a complete AFF(I-V) or CS22 gene cluster. This work enlightens the importance of whole genomic analysis to further characterize other bacteria that steel need a complete molecular definition.

14:20 -14:45	**Bile acid profiling reveals distinct signatures in undernourished children with environmental enteric dysfunction** Sean R. Moore, University of Virginia, Charlottesville, VA, USA

14-45 -15:10	**Characterizing the biochemical alterations associated with environmental enteric dysfunction using metabolomics** Jonathan Swann, University of Southampton, UK

15:10 – 15:45	**Modeling enteropathy or diarrhea with the top bacterial and protozoal pathogens: update on differential determinants of outcomes** Richard L. Guerrant, University of Virginia School of Medicine, Charlottesville, VA, USA

While enteric infections still kill over 1000 children each year (nearly 0.5 million deaths/yr in children <5 years old), they contribute significantly to such long term effects as stunting (that affects over 150 million children under 5 years old) as well as significant cognitive impairment (especially higher executive function, like that seen in patients with Alzheimer's dementia at life's other extreme, and even the costly problems of heart disease and strokes associated with metabolic syndrome in later life. Hence these 3 long-term effects may be even more costly to human development than diarrhea itself. For those we have suggested that these 3 new diseases be named: **HAZdrop** (for the stunting that occurs in a child's first 2 years of life); **COGhit** (for the cognitive impairment that can be attributed to enteric infections in early life) and **METsyn** (for the later life metabolic syndrome that can be shown to follow early life enteropathy or diarrhea). Although these are potentially objectively measurable in the field, laboratory models can help demonstrate causality and plausible signaling pathways of pathogenesis, by isolating specific determinants, such as specific pathogen infections, microbiome, diet and metabolic correlates or consequences. Linking clinical evidence with laboratory evidence can not only help establish causality, but also assess potential interventions to ameliorate these acute and longer-term consequences of the enteropathy that is so ubiquitous in children living in impoverished areas worldwide. Such is the focus of our 45-year collaboration of UFC with UVa, UFRN and UFBa.

This presentation will provide an overview of the clinical background, changes that have occurred over time, and focus on murine models of specific enteric infections that exemplify different effects by pathogen, microbiome, diet and metabolism. Examples include *Cryptosporidium*, ETEC, *Shigella*, *Campylobacter* and EPEC infections, and opposite effects of different co-infections, as well as promising vaccine effects.

16:00 -16:25	**Leishmaniasis in the semiarid area of Brazil: clinical and epidemiology** Anastácio de Queiroz Sousa, Federal University of Ceara

16:25 - 16:50	**Leishmaniasis and coinfections in dogs in the urban community of Fortaleza, Ceará, Brazil** Adam L Lima, Ph.D., Abbott Laboratories and State University of Ceara

16:50 - 17:15	**Role of immune-inflammatory biomarkers and pathobiology in leishmaniasis** Selma Jerônimo, Federal University of Rio Grande do Norte

17:15 – 17:40	**Colorimetric and fluorometric LAMP for species-specific detection of *Leishmania* spp.** Rubens Lima do Monte Neto, FIOCRUZ, MG

Nowadays we are facing disruptive technological advances including the decentralization of molecular diagnostic tools, including point-of-care (PoC) solutions. In this regard, detection of *Leishmania* spp. DNA is useful for the diagnosis of Leishmaniasis, considered one of the most neglected and serious parasitic infectious diseases. Recent reports evidenced dermotropic *Leishmania* parasites present in the visceral form of the disease, such as *L. amazonensis* in dogs suffering from visceral leishmaniasis (VL) or *L. infantum* (viscerotropic species) associated with cutaneous lesions in human patients. In or der to provide a molecular tool to differentiate among *Leishmania* spp, we designed displacing probes primers to be used in colorimetric of fluorometric LAMP (loop-mediated isothermal DNA amplification) reactions. In this talk we present some optimizations and technique validation using axenic cultured parasites and clinical samples. The test is specific with LoD at picomolar range and can differentiate among *L. infantum, L. braziliensis* and *L. amazonensis*. The colorimetric output is based on pH changes during DNA amplification and can be read using the portable PoC LAMP device OmniLAMP, recently developed by our team. The device is controlled by an App able to manager the sample input, thermal reaction and automatically interpretate the results that can be send to a data cloud. Preliminary results on the clinical validation revealed almost 90% sensitivity for detecting *L. infantum* in blood and bone marrow. For *L. braziliensis* from human-derived skin lesions, the sensitivity was 58%. Both LAMP-derived outputs in less than 2 h. Improvements of the assay are being performed associating LAMP with gold nanoparticles – here called iAnG (isothermal DNA amplification nanogold) – in order to reduce the amplification time and increase sensitivity. The solution is compatible as a portable PoC assay for the molecular diagnosis of leishmaniasis.

8:35 – 9:00	**A brief look at coronavirus pathogenesis** Eurico Arruda, State Univesity of São Paulo, Ribeirão Preto, SP

9:00 - 9:25	***SARS-CoV-2* pathobiology in mild and moderate acute human respiratory infection** Rafhaella Gondim, Federal University of Ceara

SARS-CoV-2 PATHOBIOLOGY IN MILD AND MODERATE ACUTE HUMAN RESPIRATORY INFECTION

R.N.D.G. Gondim, E.A.G. Arruda, R.J. Pires-Neto, M.S. Medeiros, J. Quirino-Filho, M. Clementino, L.M.V.C. Magalhães, K.F. Cavalcante, V.A.F. Viana, L. P. Mello, D.G.L. Lima, A.A. Santos, P.J.C. Magalhães, A. Havt, C.C. Clososki, L.L.P. Silva, N.P. Lopes, E. Arruda, A.A.M. Lima.

Respiratory tract infections are one of the leading causes of hospitalization worldwide. In late 2019, cases of pneumonia of unknown origin were reported in the city of Wuhan, China. Soon, the disease of etiology Coronavirus SARS-CoV-2, spread around the world and the COVID-19 pandemic was declared by the WHO. Several biomarkers have been evaluated as predictors of severity or to direct the treatment of COVID-19, however, to date, this relationship is not well established. In this study, biomarkers of cytokines, chemokines and cell growth factors associated with the pathobiology of COVID-19 were evaluated by Luminex technology. Samples from symptomatic patients with mild to moderate respiratory disease who sought outpatient hospital care were tested for the presence of SARS-CoV-2. Patients with negative tests for COVID-19 had their samples analyzed for other respiratory viruses (Influenza A, B and Respiratory Syncytial Virus). As a result of the analyses, it was found that a profile of pro-inflammatory cytokines such as IL-1β, IL-6, G-CSF and TNF-α was elevated in mild to moderate respiratory infections caused by SARS-CoV-2 when compared to the profile of other infections caused by seasonal respiratory viruses. All evaluated cytokines were at increased levels among COVID-19 positive patients. In addition, 5% (4/83) of samples that tested negative for COVID-19 tested positive for RSV. Finally, the data provided by the research when associated with the characterization of the pathobiology of the disease provides some mechanisms for understanding the influence of biological changes on the clinical phenotypes of COVID-19.

Keywords: Coronavirus SARS-CoV-2, COVID-19, biomarkers.

9:25- 9:50	**N-acetylcysteine: molecular mechanisms of cell preservation against inflammatory aggression of SARS-CoV-2 infection** Hugo Pequeno Monteiro, Escola Paulista de Medicina, UNIFESP, São Paulo, SP

* Hugo P. Monteiro

* Department of Biochemistry- Center for Cellular and Molecular Therapy

Escola Paulista de Medicina/Universidade Federal de São Paulo

The pandemic caused by infection with the new coronavirus SARS-COV-2, has become the biggest public health problem worldwide. Viral infection by SARS-CoV-2 causes COVID-19, a disease characterized by an acute respiratory syndrome and a hyper inflammatory reaction. Disease onset ranges from mild to severe, and to critical cases. Oxidative stress has been associated with the inflammatory reaction caused by the infection with SARS-CoV-2. The loss of antioxidant capacity in a condition of cellular oxidative stress, is mainly reflected in the decrease in the levels of reduced glutathione (GSH) and/or an increase in the levels of oxidized glutathione (GSSG). In vivo, oxidative stress mostly translates into the deficiency of GSH and/or its precursor, cysteine. The maintenance of high concentrations of GSH in all cell types demonstrates its essential participation in the control of various biological processes. Supplementation with antioxidants can neutralize the deleterious effects of an excess of reactive oxidative species (ROS). Replenishment of the cysteine stocks using a derivative of this amino acid, N-acetylcysteine (NAC), provides the conditions for maintenance of high intracellular levels of GSH. NAC has been used clinically to treat a variety of pathological conditions associated with oxidative stress, including liver toxicity caused by paracetamol, acquired immunodeficiency syndrome - AIDS caused by HIV infection, cystic fibrosis, chronic obstructive pulmonary disease, and diabetes mellitus, among others. Early studies have shown that preventive administration of NAC significantly reduces the incidence of symptoms caused by Influenza virus infection, especially in high-risk elderly individuals. In conclusion, NAC potentially could provide the means to counteract the deleterious actions of ROS derived from the inflammatory reaction associated with SARS-CoV-2 infection.

9:50-10:15	**Clinical, control, double-blind, randomized trial with N-acetylcysteine and bromhexine for COVID-19: preliminary results** Roberto J Pires Neto, Federal University of Ceara

Several therapeutic agents have been evaluated for the treatment of COVID-19, but only some have shown efficacy to reduce the duration of the disease. This research has as its primary objective (1) to determine the effect of N-acetylcysteine (NAC; reducing substance and complementary viral intercepting action) and combination of NAC + bromhexine (BMX; viral protease inhibitor), on the clinical duration of COVID-19. The study has as secondary objectives: (2) to assess the change in viral load by RT-qPCR of SARS-CoV-2 between the 1st and 4th. days of the protocol; (3) to determine the action of NAC and BMX + NAC on the immune response using the rapid ELISA test (IgM / IgG) to be performed on the 10th. monitoring day of the protocol; and (4) Assess the effect of NAC and BMX + NAC on the change in the serum level of inflammation biomarkers and reducing substances (IL-6, MCP-3, D-dimer, IL1-RA, IL-10, GCSF, TNF- α, MCP-1, IL-2R, MIP-1 alpha, IP-10, IL-8, NT-proBNP, Troponin I, PCR and procalcitonin; glutathione peroxidase-GPx; SOD and CAT) of patients collected on the 1st. and 10th. study days. The study is a prospective, double-blind, placebo control and randomized clinical trial of a total of 300 patients, with mild to moderate disease, equal to or above 18 years of age, with clinical signs and symptoms of COVID-19 confirmed by the RT-qPCR test. The study has been carried out using the Surveillance, Service and Research Network - REVAP-C19, NUBIMED, FAMED, UFC, Fortaleza, CE. The random groups of treatments are: (1) Placebo control (Vitamin C - 500 mg / day, for 10 days); (2) N-acetylcysteine (NAC; 1800 mg / day, for 10 days); and (3) NAC (1800 mg / day, for 10 days) + Bromhexine Hydrochloride (BMX; 32 mg / day, for 10 days). The study began enrollment in November 2021. As of April 2022, 234 patients were enrolled and randomized to the three groups. 118 patients completed follow up. The positivity for SARS-CoV-2 by RT-qPCR in 155 biological samples was 30.3%.

10:15-10:40	**Intestinal epithelial barrier function and SARS-CoV-2 spike glycoprotein: function and pathobiology using Ussing Chamber model in murine** José Kleybson Sousa, Federal University of Ceara

10:40-11:05	***SARS-CoV-2* spike glycoprotein triggers intestinal chloride hypersecretion and inflammation in murine model** Cristhyane Costa de Aquino, Federal University of Ceara

11:05-11:30	**Detection of SARS-CoV-2 in different human biofluids using the loop-mediated isothermal amplification assay: a prospective diagnostic study in Fortaleza, Brazil** Marco Clementino, Federal University of Ceara

We adopted the reverse transcriptase - loop mediated isothermal amplification (RT-LAMP) to detect SARS-Cov-2 in patient samples. Two primer sets for genes *N* and *Orf1ab* were designed to detect SARS-CoV-2, and one primer set was designed to detect the human gene *Actin*. We collected prospective 138 nasopharyngeal swabs, 70 oropharyngeal swabs, 69 saliva, and 68 mouth saline wash samples from patients suspected to have severe acute respiratory syndrome (SARS) caused by SARS-CoV-2 to test the RT-LAMP in comparison with the gold standard technique RT-qPCR. Accuracy of diagnosis using both primers, N5 and Orf9, was evaluated. Sensitivity and specificity for diagnosis was 96% (95% CI 87-99) and 85% (95% CI 76-91) in 138 samples, respectively. Accurate diagnosis results were obtained only in nasopharyngeal swab processed via extraction kit. Accurate and rapid diagnosis could aid COVID-19 pandemic management by identifying, isolating, and treating patients rapidly.

11:30-11:55	**Avian influenza: the new paradigm of H_5 viruses** Helena Lage Ferreira, Faculdade de Zootecnia e Engenharia de Alimentos da USP - FZEA/USP, SP, Brasil

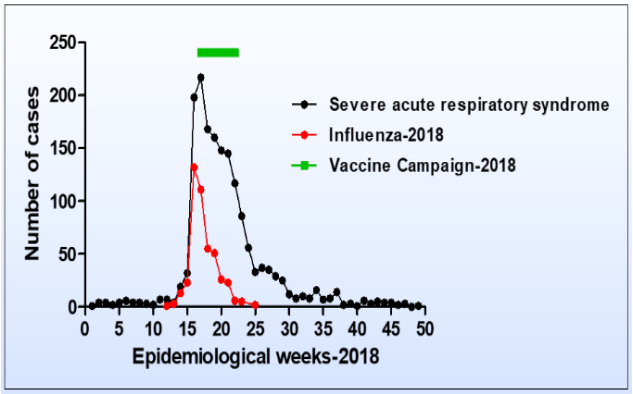
11:55 – 12:20	**Influenza in pregnancy and childbirth in the Brazilian semiarid: the INFLUEN-SA study** José Quirino Filho, Federal University of Ceara

José Q. Filho[1], Aldo A.M. Lima[1], Francisco S. Junior[1], Thaisy B.R. Lima[2], Vânia A.F. Viana[3], Jaqueline S.V. Burgoa[3], Simone A. Herron[4], Hunter L. Newland[4], Kunaal S. Sarnaik[4], Gabriel F. Hanson[4], Jason A. Papin[4], Sean R. Moore[4]

[1]Federal University of Ceará, [2]Ceará State Health Secretariat, [3]Central Public Health Laboratory of Ceará, [4]University of Virginia School of Medicine,Charlottesville, Virginia, USA.

Background - Multiple studies show that influenza during pregnancy is associated with both preterm birth and low birthweight. Previous work shows that seasonal influenza in Ceará in the Semi-Arid region of Brazil occurs 2 to 3 months earlier than in the South and Southeast. Furthermore, influenza strains in Fortaleza demonstrate higher parity with Northern hemisphere strains. *Despite these well-described epidemiological differences, all of Brazil is subject to the same vaccination schedule, hence pregnant women and their fetuses are inadequately protected against influenza in the tropical and equatorial regions of Brazil.* Using data science approaches, we will test the hypothesis that Brazil's current national policy targeting vaccination only during the months of April and May, using the Southern Hemisphere vaccine, inadequately protects against the harmful maternal-fetal effects, preterm birth, small for gestational age and underweight, of influenza in the Semi-Arid and northern regions of Brazil. **Methods** - In Phase I, we propose to leverage existing Ceará state and national databases to confirm regional variations in associations between influenza and adverse birth outcomes (preterm birth, small for gestational age and underweight) in Brazil. If Phase I is successful, in Phase II, we propose to reduce this burden by modeling and testing a modified vaccine schedule and formulation in pregnant women. We characterize the pregnant population with severe acute respiratory syndrome (SARS) by age, influenza virus and subtypes, incidence, deaths and historical lethality of cases in the state of Ceará, Brazil in the period 2013 - 2018. **Results** -In this historical series we had 3,297 cases of SARS, of which 145 (4%) were pregnant. The median age of SARS cases was 26 (15-44) years. Of the virus diagnosed cases of SARS (134), 43 (32%) were due to influenza. Of the 43 cases of influenza subtype 18 (42%) were A / H1N1 followed by 14 (33%) A H3 / seasonal, 8 (19%) influenza B and 3 (7%) A without subtype. Those of pregnant women with SRAG were 3 (100%) deaths due to other viruses or etiologic agents not specified and 0 (0%) due to influenza. **Figure 1** shows the number of cases of SARS and cases of influenza in the year 2018. Observe the peaks of SARS and concomitant influenza between the 15-20 epidemiological weeks and the vaccination period immediately after the peaks. Children preterm birth and underweight were associated with SARS in pregnancy, 2,879.1 ± 783.57 g (p = 0.019) and 16 (27%) (p = 0.025) compared to controls pregnancy, 3,195.6 ± 572.61 g and 10 (13%), respectively. The 19 SARS per influenza in pregnancy decreased birth weight (3,029.0 ± 778.24 g) and increased percentage of preterm births 4 (21%) without reach significant p values (> 0.05). **Conclusions** -These data suggest that SARS causes maternal-fetal injury resulting in low birth weight and an increase in the proportion of preterm births. The data also show that the vaccination period is after the peak of cases of SARS and influenza showing the inadequate protection of SARS and influenza seasonality.

Figure 1



13:30 - 13:55	**Gastro-esophageal reflux disease: News in pathophysiology and diagnosis** Daniel Sifrim, Queen Mary University of London, UK

13:55 -14:20	**Distal esophageal exposure is associated with inspiratory oral pressure, a measurement of the diaphragm strength, particularly in aging** Miguel Ângelo Nobre e Souza, Universidade Federal do Ceara

14:20 -14:45	**The role of Ca^{2+} signaling in the physiology and pathophysiology of exocrine pancreas** David Criddle, University of Liverpool, UK

14-45 -15:00	**Impact of the physical exercise on the gastrointestinal dysmotility** Moisés Tolentino Bento da Silva, Universidade do Porto, Portugal

15:00 – 15:15	**Activation of the ubiquitin-proteasome pathway in the crural diaphragm in reflux esophagitis** Suliana Mesquita Paula, Universidade Federal do Ceará

Paula SM, Alves MNM, Andrade MC, Silva DTC, Coutinho TAA, Nobre-Souza MAN, Santos AA

Introduction: Gastroesophageal Reflux Disease (GERD) is related with crural diaphragm (CD) insufficiency, which supports the idea of a skeletal muscle deficiency in reflux esophagitis. Skeletal muscle atrophy has been strongly associated with changes in the ubiquitin-proteasome system, considered the main proteolytic system involved in muscle atrophy. Here, we aim to assess if atrophy proteins are differently expressed in CD of patients with reflux esophagitis and if there is any relation with different grades of GERD. **Methods:** After approval by the local Ethical Committee, we obtained human CD biopsies from volunteers,15 females and 10 males, aged between 25-62 years, at the time of anti reflux laparoscopic surgery (esophagitis group - GERD) or gallbladder surgery (control group - CT). Esophagitis group was further divided in grades A (GERD-A, n=5), B (GERD-B, n=7) or C (GERD-C, n=3), according the Los Angeles scale. We studied different signaling pathways (AKT, pAKT, MuRF-1 and MAFbx/Atrogin-1, all normalized by GAPDH). Data are shown as mean ± SEM and compared by Student's *t*-test or one-way ANOVA (*,P<0,05). **Results:** Protein expressions of MuRF-1, pAKT/AKT ratio and Atrogin-1 were not different between CT and GERD groups. However, MURF-1 expression of GERD-C group (1.05 ± 0.18) differs when compared to GERD-B group (0.27 ± 0.11). CT group was not different from GERD-A and GERD-B groups. Furthermore, there was a close relationship between total reflux time (supine position) and MURF-1 expression (r=0,701; p<0,05). **Conclusion:** GERD-C patients had increased expression of MURF-1, a protein considered as a potential marker of skeletal muscle atrophy, and this was associated with increased total reflux time in supine position. These findings provide a potential molecular mechanism underlying the development of diaphragm fiber atrophy and weakness in these patients, being a potential contributing factor to the worsening of lower esophageal sphincter tone reduction and to the formation of a self-perpetuating cycle of GERD. Additional upstream and downstream signaling pathways to increase MuRF-1 expression are yet to be clarified.

Keyword: GERD, Crural diaphragm, Atrophy.
Financial support: CAPES, CNPq.

15:15 – 15:40	**Role of bile acids in the contractile activity of rat esophageal segments** Kaline Kelly Lima Gadelha, Universidade Federal do Ceara

Kalinne Kelly Lima Gadelha,[1] Karine Lima Silva,[1] Armênio Aguiar dos Santos, [1] Pedro Jorge Caldas Magalhães[1]

[1] Department of Physiology and Pharmacology, School of Medicine, Federal University of Ceara, Fortaleza, CE, Brazil

ABSTRACT

Gastroesophageal Reflux Disease (GERD) is a pathology of multifactorial origin and high prevalence worldwide, originated from anatomical and physiological causes. For a long time, acidity was considered as the main mediator of esophageal injury, but nowadays it is known that other components are relevant, such as bile acids, which have been documented in high concentrations in the esophageal lumen of patients with the disease. Abnormal patterns of esophageal body motility may be found in patients with GERD and a role for bile acids in the pathobiology of the disease has been debated. The present study evaluated the effects of exposing rat esophageal segments to bile acids and their contractile repercussions. Preliminary results revealed that luminal exposure of rat esophagus to acidic solution enriched with pepsin and taurodeoxycholic acid (TDCA) impaired the contractile response of isolated esophageal strips. Focusing on the bile acid actions, a direct challenge with deoxycholic acid (DCA) or TDCA reduced the contractions caused by the muscarinic agent carbachol. In the presence of oleanolic acid, an agonist of the G protein-coupled bile acid receptor (GPBAR/TGR5), a significant reduction of the contractile activity of the esophageal strips was observed. Previous addition of triamterene, a compound that has been recently investigated as an inhibitor of the TGR5 receptor, attenuated the inhibitory influence caused by DCA against carbachol. A similar effect was seen with the adenylate cyclase inhibitor – MDL 12330A. Our findings suggest that bile acids interfere with esophageal contractility in rats, possibly acting on TGR5 receptors.

Financial support: Instituto De Biomedicina Do Semi-Árido Brasileiro (IBISAB), Conselho Nacional de Desenvolvimento Cientifico e Tecnológico (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) and Fundação Cearense de Apoio ao Desenvolvimento Científico e Tecnológico (FUNCAP) of Brazil