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X Seminar - PhD Day

Science for Democracy - Democracy for Science

Istituto Superiore di Sanità
Rome, May 17 2019

ABSTRACTS BOOK

Edited by
A. Rosso, G. Napoletani, S. Buezo Montero,
A. Pizzarelli, V. Perri, R. Tittarelli,
L. Amato, A. Mazzaccara

ISTITUTO SUPERIORE DI SANITÀ

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Edited by
Annalisa Rosso (a), Giorgia Napoletani (a),
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The 10th Meeting of PhD students in Infectious Diseases, Microbiology and Health Sciences will be focused on the difficult and controversial relationship between democracy and science. While the lack of knowledge-sharing behaviour can jeopardize the credibility of scientists, on the other hand scientific data must be subjected only to rigorous validation and verification, not to public judgement or to the appeal for the wide audience. We would like to deepen the connections between democracy and science, a topic of particular concern in Public Health.
Key words: Science, Democracy; Microbiology, Comunicable Diseases, Public Health, Social Medicine, Forensic Medicine

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La decima Giornata dei Dottorandi in Malattie infettive, microbiologia e sanità pubblica si concentrerà sul difficile e controverso rapporto tra democrazia e scienza. Se da un lato la mancanza di un comportamento disponibile alla condivisione dei dati scientifici può diminuire la credibilità dei ricercatori, dall'altro la scienza deve essere sottoposta al solo controllo di validazione e verifica da parte di esperti e non al giudizio popolare o al consenso del grande pubblico. Cercheremo quindi di approfondire le connessioni tra il cittadino, la scienza e la democrazia, specialmente in un contesto, come quello della Sanità Pubblica, dove il coinvolgimento della popolazione appare di importanza primaria
Parole chiave: Scienza, Democrazia, Microbiologia, Malattie Infettive, Sanità Pubblica, Medicina Sociale, Medicina Legale

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PREFACE

After so many editions, the PhD Day represents a traditional, successful event in the activities of the PhD in Infectious diseases, microbiology and public health.

The presentation of the research activities of the PhD students will span through the main themes that characterize our PhD, including hygiene, social medicine and public health, infectious diseases as clinical application of basic science studies on virology, bacteriology and parasitology as well as legal medicine, forensic toxicology and environmental chemistry.

As usual, the PhD students of the third year will present orally their results, while students at the second year will present their studies as a poster. This will permit to a wide audience to get in touch with the most updated researches in the field.

Beside to the presentations of the PhD students, two topics will be discussed as opening lectures of the two sessions, one focused on vaccine hesitancy and another on the historical outline of the Spanish flu after 100 years from the pandemic events of 1919.

The PhD day will be opened, as it is traditionally made since several years, by a Lectio Magistralis entitled “Science is democracy”. This is an actual, fascinating, but controversial theme, that will raise up, we believe, debate and comparison of different opinions.

The scientific Staff

Laura Amato, Sara Buezo Montero, Massimiliano dell’Aquila, Alfonso Mazzaccara, Giorgia Napoletani, Silvio Paone, Paolo Pavone, Valentina Perri, Antonella Pizzarelli, Luigi Rosa, Annalisa Rosso, Nordino Ibraimo Sulemane, Roberta Tittarelli

PROGRAMME

May 17, 2019

9.00 Registration

9.20 Preliminary welcome:
Silvio Brusaferro, Carlo Della Rocca,
Ciro Villani, Paolo Villari, Stefano D'Amelio

9.50 Lectio magistralis
Scienza è democrazia
Maria Luisa Villa

Session 1
HEALTH SCIENCES, ENVIROMENTAL CHEMISTRY, SOCIAL MEDICINE AND FORENSIC MEDICINE

Chairpersons: **Silvia Canepari, Silvia Declich, Carolina Marzuillo**

10.30 Lecture
Vaccine hesitancy e percezione del rischio: una spiegazione neuroevolutiva
Andrea Grignolio

11.00 Poster session and new research topics
Coffee Break

PhD candidates' communications

11.30 *Pilot project to set up a centre for preventive medicine and health care for students of medicine and health professions of the University of Rome*
Rosella Saulle

11.45 *The role of CardioMicroRNAs in timing of early myocardial infarction: medico-legal evaluation and translational medicine implication*
Natascha Pascale

12.00 *Quantifying the impact of adherence to screening strategies on colorectal cancer incidence and mortality*
Elvira D'Andrea

12.15 *Neuroimaging of psychopathy: functional MRI alterations in socially dangerous patients with diminished penal responsibility*
Gaia Cartocci

12.30 *Social capital and students' health - an international study*
Insa Backhaus

12.45 *Morphological research and relationship between biomarkers and oxidative stress in brain trauma and in hypoxic-ischemic injuries*
Luigi Cipolloni

13.00 *Human enhancement: bio-juridical issues*
Lidia Ricci

13.15 Lunch

14.00 *Exploring self-care process in Iranian women with breast cancer. A grounded research approach study*
Somayeh Mahdikhani

14.15 *Socially dangerous psychopathic patients NGRI: a case control study to evaluate risk factors for recidivism*
Pieritalo M. Pompili

Session 2
INFECTIOUS DISEASES, MICROBIOLOGY AND PARASITOLOGY

Chairpersons: **Serena Cavallero, Alessandra Oliva, Daniela Scribano**

14.30 Lecture
100 years after the Spanish flu: a lesson from history, a clue for the future
Anna Teresa Palamara

PhD candidates' communications

15.00 *Study of the prevalence of Anisakis hypersensitivity in professionally exposed populations*
Antonella Costa

15.15 *Type I/II interferon in HIV-1 infected patients: expression in gut mucosa and in peripheral blood mononuclear cells and its modification upon probiotic supplementation*
Claudia Pinacchio

15.30 *Nuclear Magnetic Resonance based-metabolomics analysis of urine in HCV patients with severe liver fibrosis receiving direct-acting antiviral agents*
Donatella Palazzo

15.45 *Evaluation of antimicrobial activity of the essential oil and nano-emultions from* Satureja montana*,* L. Lamiaceae
Luca Vitanza

16.00 *The human GTP-ase RAC 1 plays an important role in* Plasmodium falciparum *infection of human erythrocytes*
Silvio Paone

16.15 *The effect of HSV1 recurrent infection on modulation of age-related epigenetic markers*
Giorgia Napoletani

16.30 *Speckle Tracking Echocardiographic assessment of patterns and distribution of ventricular strain impairment in young adults with human immunodeficiency virus infection*
Lidia Capotosto

16.45 *Cardiovascular risk and coronary stenosis are easily underestimated in HIV infected subjects*
Eugenio Nelson Cavallari

17.00 Conclusions
Stefano D'Amelio

Session I

Health sciences, environmental chemistry, social medicine and forensic medicine

Chairpersons:

Silvia Canepari, Silvia Declich, Carolina Marzuillo

SOCIAL CAPITAL AND STUDENT'S HEALTH AN INTERNATIONAL STUDY

Insa Backhaus, Giuseppe La Torre
Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

Background. Increasingly, universities across the world are reporting rising rates of health problems and mental disorders. The variations in the rates of health problems between different geographical regions suggest that specific social causes may play a role. Because social capital is believed to play a significant role in well-being, mental health and lifestyle choices, it is valuable to study their relationship in the context of university students. The purpose of this study was to investigate student's mental health status from different countries and to explore whether there is an association between social capital and depressive symptoms.

Methods. A cross-sectional study was conducted in Albania, Germany, Italy, Switzerland, Brazil, Oman, Malaysia, Taiwan, South Korea, and the USA in 2018. For each population information on gender, age, quality of life, perceived stress, depressive symptoms and lifestyle habits was gathered through self-administered questionnaires. Descriptive and inferential statistical methods were applied. Chi-square test and Mann-Whitney U test were used to describe the sample and to compare characteristics between students of each country. Multilevel analyses were performed to assess the association between social capital and depressive symptoms while controlling for the effects individual level characteristics.

Results. Almost 19% of students rated their health as fair/poor and nearly 24% of students have had suicidal thoughts at least once. Around 40% of students demonstrated clinically relevant depressive symptoms. Analyses showed that depressive symptoms and social capital are correlated, with students who have lower levels of social capital having higher odds to have clinically relevant depressive symptoms.

Conclusions. This study is among the first to analyze social capital and student's health from diverse countries. The findings showed that social capital still remained associated with depressive symptoms even after adjustment for potential confounders. Nonetheless, as with every cross-sectional study inference about the temporal ordering of the variables cannot be made. Furthermore, the influence of other lifestyle factors and contextual factors (e.g. low-income country) still needs to be further investigated. Social capital may act as one of the most important predictors of mental health of university students. The results help to understand when and for whom there is an increased risk for a mental health disorder. The influence of certain lifestyle factors as well as contextual factors, however, remain to be investigated. Given the high prevalence of mental health problems among students, universities and policy makers may want to start considering policies that can strengthen social capital.

NUROIMAGING OF PSYCHOPATHY: FUNCTIONAL MRI ALTERATIONS IN SOCIALLY DANGEROUS PATIENTS WITH DIMINISHED PENAL RESPONSIBILITY

Gaia Cartocci (a), Paola Frati (a), Francesca Caramia (b)
(a) Department of Anatomical, Histological, Locomotor and Legal Medicine Science, Sapienza University of Rome, Rome, Italy
(b) Human Neuroscience, Sapienza University of Rome, Rome, Italy

Background. In this exploratory study we investigate differences in brain network underpinning moral judgment, salience attribution and reward, by using resting state functional connectivity in an MRI study on a population of prison inmates detained in the psychiatric unit of Residences for Execution of Security Measures (REMS) and healthy age and gender-matched healthy participants, without history of neurological/psychiatric disorders and crimes.

Methods. The study included 13 adult male prison inmate participants (Experimental Group, EG: mean age 44 yrs; SD 7 with a documented history of severe criminal offense. Control Group (CG) included 13 healthy men (mean age 38 yrs; SD 11) who never received a psychiatric diagnosis or undergone any psychiatric treatment and were never convicted for crimes. MRI data were acquired using a 3 Tesla Siemens imaging system; resting state functional (rs-fMRI) data were collected while participants lay still and awake, with eyes closed. The rs-fMRI data were preprocessed using CONN v. 18a, running in Matlab.

Results. As compared with CG, EG showed a remarkable increased functional connectivity in left hemisphere between FOrb and putamen (t_{24}= 3.272; p=0.003), FOrb and pallidum (p=0.006), pallidum and amygdala (p=0.001), PC and nucleus accumbens (p=0.017), AC and caudate (p=0.022) caudate and putamen (p=0.020), putamen and pallidum (p=0.019).In EG, we also found increased functional connectivity between left and right putamen (p=0.029) as compared with CG. Otherwise, in the CG we found higher functional connectivity in the right hemisphere between AC and caudate nucleus (p=0.040) than EG. The Social behavior is related to morality, which might be considered as the sets of customs and values to guide a social conduct. Abnormal moral behaviour implies the violation of ethical rules and civil rights and often results in violence and criminal acts. We found that EG showed increased connectivity in subcortical network, particulary in brain regions involving reward processes, salience and moral judgment. Cortico-striatal circuit dysregulation drives maladaptive decision making in psychopathy, supporting the notion that reward system dysfunction comprises an important neurobiological risk factor for predicting criminal convictions and recidivism.

Conclusions. These initial results will deserve future investigation: assessing culpability in mentally disordered offenders poses complex challenges for both lawyers and psychiatrists. Furthermore, the multidisciplinary approach will provide innovative information over current state of the art, improving the knowledge about neural correlates of psychopathy and for treatment development.

MORPHOLOGICAL RESEARCH AND RELATIONSHIP BETWEEN BIOMARKERS AND OXIDATIVE STRESS IN BRAIN TRAUMA AND IN HYPOXIC-ISCHEMIC INJURIES

Luigi Cipolloni, Benedetta Baldari, Paola Santoro, Livia Besi
Department of Anatomical, Histological, Locomotor and Legal Medicine Science, Sapienza University of Rome, Rome, Italy

Background. The head trauma and hypoxic-ischemic encephalic injuries are a major cause of death whose framework are taken into account the neurological characteristics and the changes identified with CT and MRI. In the literature it was demonstrated the existence of a fairly precise chronology of expression of different markers of cerebral hypoxic-ischemic injury due to a stimulation of different cell types and to a different response from the ischemic insult cells. Oxidative stress plays a major role in the genesis of delayed adverse effects that contribute to permanent damage.

Methods. Our study research evidence about the correlation between genetic variants, extent of brain injury and clinical outcome after TBI. An important area of research is the identification of the period of hypoxic-ischemic injury to the assessment of the causal link and any responsibilities with the methodological rigor of their discipline, articulated by means of: - an examination of the medical records and imaging studies; - pre-post-mortem radiological study; - Autopsy complete with biological samples; - complete histological investigation.

Results. An autopsy is the Prince survey and its value is enhanced with the help of appropriate toxicological investigations, microbiological, genetic and histological. Particular attention should be paid to the research of cell changes after the hypoxic-ischemic and whose precise history is well known in the literature. Upon completion of the routine histopathological reading, using new immunohistochemical type searches for the detection of proteins or enzymes expressed at brain level in subsequent stages to a traumatic event/hypoxic-ischemic. In order to find reliable markers, objective and repeatable, which anchor the judgment on the age verification pathological insult, we will proceed to the review of a large series of autopsy surveys conducted at the Institutes of the Universities and Research Centers. The brain samples represented by cortical levies, basal ganglia and brainstem, will be sectioned and stained with hematoxylin-eosin accompanied by argentic, Perls and Von Kossa. For the next immunohistochemistry will be used an antibody panel based on the most recent scientific literature on the subject of damage brain, directed against: GFAP, TNF, IL1, IL-6, MAC387, HSP 27, 70 and 90, COX2, ORP150, b-APP, Tryph, GAP-43, apoptosis (TUNEL-TdT enzyme).

Conclusions. The application of this methodology would allow to identify immunohistochemical markers for evaluating the timing of brain damage.

QUANTIFYING THE IMPACT OF ADHERENCE TO SCREENING STRATEGIES ON COLORECTAL CANCER INCIDENCE AND MORTALITY

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(c) School of Medicine and Gastroenterology of the Rockies, University of Colorado, Denver, CO, USA

Background. Current recommendations of The US Preventive Services Task Force (USPSTF) and other clinical guideline groups on colorectal cancer screening strategies are based on models that assume full (i.e. 100%) adherence to screening. Since adherence can substantially affect the outcomes of a screening modality and cancer incidence is a key outcome for cancer prevention, we aimed to assess the comparative outcomes of different screening strategies under published estimates of actual adherence rates, estimating both cancer incidence and mortality.

Methods. We developed an individual-level simulation model which replicates the natural history of colorectal cancer. After validation against landmark trials and USPSTF models, we evaluated the effectiveness of colonoscopy (COL), flexible sigmoidoscopy (FS), high-sensitivity guaiac faecal occult blood test (HS-gFOBT), faecal immunochemical test (FIT), multitarget stool DNA test (FIT-DNA), computed tomography colonography (CTC), and the FDA-approved version of the methylated SEPT9 DNA test (SEPT9) in reducing colorectal cancer (CRC) incidence and mortality. For each screening strategy, we also estimated the incremental life-years gained, number of colonoscopies and other tests, and adverse events. The assessment was performed under both the assumption of full adherence and reported adherence rates.

Results. Assuming full adherence, FIT-DNA, FIT, HS-gFOBT, and SEPT9 every year averted 58 to 59 CRC cases and 28 CRC deaths; COL and CTC strategies 55 to 56 CRC cases and 27 CRC deaths, while FS averted 39 cases and 19 deaths per 1,000 individuals. Life-years gained were similar across FIT-DNA, FIT, HS-gFOBT, SEPT9, CTC, and COL strategies. The total number of colonoscopies was highest with COL (3,567), followed by SEPT9 (3,231), HS-gFOBT (2,584), FIT-DNA (2,079), FIT (2,067), CTC (1,691) and FS (1,538). Assuming reported adherence rates, SEPT9 averted 54 CRC cases and 26 CRC deaths, followed by COL with 49 CRC cases and 24 CRC deaths, and FIT-DNA, FIT, CTC and HS-gFOBT with approximately 36 to 41 CRC cases and 18 to 21 CRC deaths averted per 1000 individuals screened. Life-years gained reflected the effectiveness of each strategy in reducing CRC cases and deaths.

Conclusions. Adherence is a key factor in determining the effectiveness of CRC screening, and the introduction of strategies with higher expected adherence rates has the potential to improve screening outcomes, including cancer incidence and mortality.

EXPLORING SELF-CARE PROCESS IN IRANIAN WOMEN WITH BREAST CANCER. A GROUNDED RESEARCH APPROACH STUDY

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Background. This study explores the prosses of self-care in the women with Breast Cancer (BC) in order to develop a model useful for better health care intervention.

Methods. This was an exploratory qualitative design through Grounded theory methodology. A purposive sample of 15 Women with BC with or without mastectomy with different experiences of self- care related to age, marital status, education, socio-economic status, employment status, duration and severity of disease who were attending a cancer clinic in Iran were recruited. Study data were collected through semi-structured interviews and analyzed using the Corbin and Strauss process and Grounded Research methodology approach.

Results. Continuous and comparative analysis of the data showed that the main concern of the participants in this study was the Fear of not Performing the role as a woman in the family. This concern was included Financial Charge of The Disease, inability, self-change, Mental Turbulence, Disrupted Social Connectedness, Inefficient health system, Unaware of the diagnosis and treatment process, Cultural influences, Sexual dysfunction and created by flowing the effect of disease on physical, emotional, mental, and social aspects of their lives. However, patients tried to achieve "autonomy" in self-care with "Trying to do self-care independently for overcome the consequences of disease". If the efforts of patients to self-care increased their caring needs, patient's self-care were acting independently, but with the exacerbation of the disease and as a result, the patients became weaker in various aspects of physical, psychosocial, and even social, patient care needs also increased so that they could not independently act on self-care. As a result, they were faced with "increasing dependence on others" in self-care.

Conclusions. Given the challenges of self-care, health care providers, especially nurses, can support women with BC in their self-care autonomy. On the other hand, the results of this study by expressing important concepts and creating a fundamental knowledge in the self-care process of women with BC can be used to formulate policies and standards of care of these patients.

THE ROLE OF CardioMicroRNAs IN TIMING OF EARLY MYOCARDIAL INFARCTION: MEDICO-LEGAL EVALUATION AND TRANSLATIONAL MEDICINE IMPLICATION

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(b) Department of Morphology, Surgery and Experimental Medicine University of Ferrara

Background. Myocardial Infarction (MI) is a major cause of mortality and disability in the world and represents an outcome measure in quality programs in health systems. In the clinical practice, the diagnosis of early stages of myocardial ischemia, within 6-8 hours ischemic insult, in which they are not yet clear histomorphological signs, it remains an unsolved problem.

Methods. The goal of this research is to detect and quantify the expression of miR-1, miR-133a, miR-499 and miR-208a on cardiac tissue samples from subjects who died of MI, in the first 6 hours of the onset of clinical symptoms, attributable to myocardial ischemia.
The casistic has been selected from autoptic cases of the Section of Pathology Forensic University of Foggia, and they have been chosen 6 cases with a well-defined clinical course (clinical symptoms, ECG and laboratory data), and in which post-mortem examination confirmed the diagnosis of MI. The patients had a survival time ranging from 0–6 hours. For each case, we will study the cardiac tissue samples (7 standard samples), collected in the course of autopsy and preserved in formalin, on which will be made the dosages of the following miRNAs: miR-133a, miR-208a, miR-499a, miR-1. At the same time, as a control test, in each cases selected it has been measured the dosage of ubiquitously expressed in the cardiac tissue, miR186 and miR361, independent of pathological condition, age, gender. Therefore, the expression of the dosed miRNAs was compared with the expression of the control miRNAs.

Results. The results obtained indicate a significant greater expression of the miRNAs dosed with respect to the control miRNAs, as the following average: miR-133a is expressed 1,7 more than miR186 and 4,2 than miR361; miR-208a is expressed 7,1 more than miR186 and 16,9 than miR361; miR-499a is expressed 1,5 more than miR186 and 3,7 than miR361; miR-1 is expressed 3,1 more than miR186 and 7,4 than miR361.

Conclusions. The next step of the study it will be evaluate the expression of the miR-133a, miR-208a, miR-499a, miR-1, in the patients died for MI after 6 hours, to ascertain significant differences of the expression, respect the timing.

SOCIALLY DANGEROUS PSYCHOPATHIC PATIENTS NGRI: A CASE CONTROL STUDY TO EVALUATE RISK FACTORS FOR RECIDIVISM

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Background Since 2008 people considered Non-Guilty in Reason of Insanity (NGRI) and socially dangerous, are sectioned in the residential forensic units called R.E.M.S (Residences for Execution of Security Measures), exclusively managed by health operators, without policemen support. In judiciary laws, social danger is considered as the risk for a person to commit future crimes in reason of mental disorder. For this reason, the assessment of mental and behavioral parameters is fundamental to connect clinical facets with recidivism and to predict the risk of violence. Violent behavior can occur in Psychosis and Mood Disorder, often in acute phases, whereas is very common in about 80% of people Personality Disorder, above all Borderline and Antisocial too. Literature suggest that Psychopathy represent the trans-dimensional clinical condition that correlates with longer criminal careers and high level of violent behavior. In fact, psychopathic suffer from a profound affective deficit, including shallow emotion and inability to experience empathy, guilt or remorse.

Methods We developed a protocol to assess both psychological and biological aspects in patients admitted in R.E.M.S. of Mental Health Department of ASL Rm5 in order to evaluate neurocognitive/psychiatric pathways and to compare differences between psychopathic and non-psychopathic groups. Psychopathy assessment require PCL-r, that is the gold standard reference scale. Case and Control are adults male 20 admitted in REMS since 2016, classified as psychopathic if their PCL-r scores is $\geq$ 20. All participants underwent clinical evaluation and MRI (Magnetic Resonance Imaging) study with specific sequences to examine possible dysfunction in neural connectivity.

Results Preliminary results demonstrate that psychopathic participants (7 adults, mean age: 42, 71 yo, PCl-r: 23,92) had many lifetime's criminal records, while non-psychopathic (6 adults, mean age 46,17 yo, PCL-r: 10,35) are admitted in forensic units for the first time in their life. First results suggest that PCL-r total score represent the most important pathway to predict recidivism of violent acts, measured with Harm-FV (Hamilton anatomy of Risk Management - forensic version), instead of PD (psychopathic deviation) scale of MMPI-II that appears elevated in both groups, without differences between psychopathic and non-psychopathic. Moreover, psychopathic traits may be correlated with different patterns of atypical neural connective activity.

HUMAN ENHANCEMENT: BIO-JURIDICAL ISSUES

Lidia Ricci, Maria Valeria Rosati
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Background. Human Enhancement is a modification aimed at improving individual human performance through scientific or technological interventions in the human body aimed to change the physique appearance, to increase the physique and the athletic performance, to intensify the working capabilities. The purposes of our study are to identify the ethical and juridical, medical legal and medical social frames, in which to assimilate the enhancement, considering that it's inevitable, because being humans are naturally competitive. Therefore, we need to value if the application of the enhancement technologies is harmful of the human dignity or if it's a useful tool to improve the human life's condition.

Methods. At first we focused on the bibliographic research dedicated to the HE's classification through the terminological analysis going into the historical and evolutionary lecture of health's and enhancement's definitions, confronting with the bio-juridical perspective as for example the possible negative effects over a person's dignity, identity, freedom, equality; and comparing scientific and humanistic theories. We later examined in detail the national and the supranational legal framework of the last ten years, from the Science and Technology Options Assessment's Human Enhancement Study to the Comitato Nazionale per la Bioetica's opinions. Starting from this classification we located and analyzed some typologies of enhancement, using a medical social methodological approach and deepening each subject matter from both doctrinaire and jurisprudential profile.

Results. Doping, cosmetic surgery and prenatal genetic enhancement's prohibition are techniques already disciplined. Smart drugs and deep brain stimulation are techniques already disciplined for therapeutic purpose, but sometimes their application lies outside the disease's therapy. Military and biological enhancement are techniques in an experimental phase. We have represented the particular difficulties in identifying the limits of lawfulness of each of these typologies of enhancement. Throughout the study we carried out, it appears essential for the law to be able to keep up with the times; but it's desirable that also the frenetic development of scientific research is in step with the respect of the ethical and juridical principles of being human.

Conclusions. We could hypothesize a 'case by case' law's approach, because it's ductile and able to adapt on the peculiar characteristics of every single form of enhancement, evaluating at the same time political, legal, ethical, social and safety impact, in a context of inhomogeneity of the Human Enhancement Technologies that it doesn't allow an uniform normative framework able to fully satisfy individual and collective needs.

PILOT PROJECT TO SET UP A CENTRE FOR PREVENTIVE MEDICINE AND HEALTH CARE FOR STUDENTS OF MEDICINE AND HEALTH PROFESSIONS OF THE UNIVERSITY OF ROME

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Background. “Sapienza" University of Rome is the largest University in Europe, welcoming students from all over Italy and Europe. The focus of this project is on 3504 students of the Faculty in Medicine, considered the most exposed in their technical and practical activities. About 60% of these students left their families’ home and city. Not rarely they deal with many difficulties especially due to the independent management of their own health (hence the loss of contact with their family physician). Often these subjects begin with unhealthy lifestyle habits that act as a source of stress negatively influencing their academic achievement on health and quality of life.

Aim. The project provides the establishment of a pilot center of preventive medicine and health care that can contributes to protecting health and the quality of life of students, through the establishment of a) a department of Preventive Medicine with expertise in vaccinations for health workers and lifestyles b) a General Medicine Service c) the creation of a website dedicated to these issues. Data about lifestyles were collected using a self-administered questionnaire, including a validated Food Frequency Questionnaire, (FFQ), which included 12 items corresponding to the12 main dietary groups: carbohydrates, vegetables, fruit, extra virgin olive oil, white meat, red meat, fish, eggs, cheeses, ham and salami, legumes and sweets. The adherence to the Mediterranean Diet (MD) was appraised according to a scale of 0-12.

Results. The results of a preliminary investigation, comprising 220 participants, showed that non-resident students had more difficulties to contact their Family Physician. Therefore, these students are more interested in the use of the service including the website that is active since July 2017. With the beginning of the University, students often engage in unhealthy lifestyles, especially worsening in eating habits. The average MD score was 7 (23.0%). While a 41% reached a score under ≤ 6, indicating that they did not adhere to MD; 37% exceeded a score of 8, adhering to it in varying degrees. Only 3.7% reached the maximum score of 11. Around 46% noticed a change in eating habits as well as changes in the body weight (23.6%) since they started University. Those changes are quite linked to the beginning of University courses for 12.3% and absolutely linked for 3.3%. 46% declares 10min daily walk, 64% spends more than 4h/day sitting. Concerning tobacco smoking exposure 54% declares significant exposure to passive smoke, 36% are current smokers and 82% thought about quit smoking.

THE OUTBREAK OF FENTANYL-RELATED DEATHS IN COOK COUNTY, ILLINOIS. A RETROSPECTIVE STUDY AND A COMPARISON WITH PREVIOUS DATA

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The National Institute on Drug Abuse in the U.S. has observed an increase in the deaths from synthetic opioids (mainly fentanyl) in recent years. Several epidemics related to the illicit abuse of fentanyl and its analogs have been reported in the Country: one of those happened in Cook County in 2005-2007 (350 individuals). Another outbreak of fentanyl death occurred in 2015-2017 in the same area. The electronic database of the Cook County Medical Examiner's Office in Chicago was searched for cases of death involving fentanyl and fentanyl analogs toxicity between October 2015 and December 2017.

A total of 27,131 deaths were identified in the studied period. Among these, 1,244 cases (4.5%) satisfied the requirements of the study. The population was divided into two subpopulations: 927 deaths involving fentanyl and 317 deaths involving fentanyl analogs (without fentanyl). Most of the cases involved Caucasian males. The mean age was 44 years old, and the study population ranged between 14 and 77 years. The mean fentanyl concentration in post-mortem peripheral blood was 18.19 ng/ml (range: 0.11-464). A progressively increasing number of cases/year was observed from 2015 to 2017: 56 in October-December 2015, 540 in 2016 and 648 in 2017. In the vast majority of 2015-2017 fentanyl cases, fentanyl was associated with other products: the most common drug used with fentanyl was heroin, followed by cocaine and ethanol.

Statistical comparisons with the 2005-2007 population were performed, showing an increase in the number of cases by 2.6 times. In both the 2005-2007 and 2015-2017 populations, the majority of deaths involved males, but a significant increase in the number of females was observed in the 2015-2017 group. Regarding the race of the decedents, in 2005-2007 the majority of deaths occurred among African Americans, while in 2015-2017 the majority of deaths involved Caucasians. In addition, some combinations of drugs were significantly more common in specific demography subgroups (male/females; Caucasian/African American; certain age groups): this could be due to an increased use/choice of these combinations in these groups, or to a possible greater susceptibility of these groups to the effect of some specific drugs association.

Knowledge about the new fentanyl outbreak could be useful for public health in monitoring and quickly diagnosing and treating acute intoxication when fentanyl is involved. Moreover, the analysis of the recreational drugs usually combined with fentanyl can contribute to a better-informed public policy that helps reduce the risk for drug abusers.

Session II

Infectious diseases, parasitology and microbiology

Chairpersons:

Serena Cavallero, Alessandra Oliva, Daniela Scribano

SPECKLE TRACKING ECHOCARDIOGRAPHIC ASSESSMENT OF PATTERNS AND DISTRIBUTION OF VENTRICULAR STRAIN IMPAIRMENT IN YOUNG ADULTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION

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Background. The aim of the study was to assess biventricular parameters of wall deformation with Three-Dimensional Speckle Tracking Echocardiography (3DSTE) in patients with human Immunodeficiency Virus Infection (HIV) on antiretroviral therapy in order to detect a possible subclinical myocardial dysfunction. A second aim was to compare these changes with the 3DSTE findings in patients with idiopathic non-ischemic dilated cardiomyopathy and systo-diastolic dysfunction to better understand the magnitude and distribution pattern of ventricular strain impairment in HIV-infected patients.

Methods. Nineteen patients aged 12 to 35 years with HIV acquired early in life, 19 normal controls of the same age and sex, and 19 patients with idiopathic non-ischemic Dilated Cardiomyopathy (DCM) were studied with 3DSTE. All HIV patients were stable in terms of HIV infection, with no history of heart disease or other chronic systemic disease except HIV infection. Patients were on HAART with good immunological control. Standard echocardiographic measures of LV-RV function were assessed. LV-RV Global Longitudinal Strain (GLS), Radial Strain (GRS), and Global Area Strain (GAS) were calculated.

Results. LV GLS and GAS were significantly lower in HIV patients compared to normal controls. There were no significant differences in LV ejection fractions between the groups. There was a weak negative correlation between LV GLS and CD4 T-cells count ($r=0.307$, $p=0.046$). DCM patients had more marked and widespread reduction in LV GLS compared to controls, whereas in HIV patients LV LS impairment ($p<0.01$) was more localized in basal and apical regions. RV free-wall longitudinal strain was significantly reduced in HIV patients when compared with the control group. No patient had pulmonary systolic pressure higher than 35mmHg.

Conclusions. Three-dimensional speckle tracking echocardiography may help to identify HIV patients at high cardiovascular risk allowing early detection of biventricular dysfunction in the presence of normal LV ejection fraction and in the absence of pulmonary hypertension. LV strain impairment in HIV patients is less prominent and widespread compared to DCM patients.

CARDIOVASCULAR RISK AND CORONARY STENOSIS ARE EASILY UNDERESTIMATED IN HIV INFECTED SUBJECTS

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Background. Pathophysiology of coronary atherosclerosis in HIV infected subjects has not been fully elucidated but specific risk factors such as HIV itself, increased immune activation or antiretroviral therapy play a role in the onset and progression of atherosclerotic plaques. Conventional tools used in clinical practice could not be adequate to evaluate cardiovascular risk in HIV infected subjects with the risk of an underestimation of the actual risk. Coronary CT angiography allows an accurate morphologic evaluation of coronary atherosclerosis and the identification of candidates to Percutaneous Transluminal Coronary Angioplasty (PTCA). Moreover, coronary calcium score is an accurate measure of cardiovascular risk

Methods. In this interventional longitudinal study, young and cardiologically healthy (Framingham score <10%, no alterations at ECG and echocardiography, no diagnosis of metabolic syndrome) HIV infected subjects were enrolled. Participants underwent clinical evaluation of cardiovascular risk following 3 different scores (Framingham, Atherosclerotic Cardiovascular Disease score, D:A:D risk calculator), blood sampling to evaluate high sensitivity C Reactive Protein (hsCRP), carotid Intima-Media Thickness (IMT) and CT coronary angiography with calcium score evaluation following the Agatston equation. Individuals with coronary vessel stenosis >50% at CT coronary angiography underwent classic angiography, as in routine clinical follow-up.

Results and Conclusions. 55 HIV infected subjects (46 men and 9 women, mean age 47.6±8.7), 49 of which on antiretroviral therapy since a median of 9.4±5 years, were enrolled. Relevant coronary stenosis (>50% vessel lumen) were observed in 29% of the study population. The presence of multiple stenosis was observed in participants with relevant coronary obstruction ($p=0.026$). In 43.8% of cases, relevant stenosis was associated with non-calcified plaques. Exposure to antiretroviral drug abacavir was associated with a greater extent of coronary plaques ($p=0.005$); duration of abacavir exposure was higher in participants with relevant stenosis ($p=0.023$). Moreover, 76.3% of participants with coronary stenosis of any grade was exposed to protease inhibitors (vs. 35.2%, $p=0.035$). Calcium score was significantly higher in subjects with relevant stenosis ($p=0.016$) and associated with the grade of stenosis ($r=0.539$, $p<0.001$). Then again, 38% of subjects with a negative calcium score showed non-calcified coronary stenosis, 11% of which were clinically relevant. IMT was higher in individuals with relevant coronary

stenosis ($p=0.002$) as well as correlated with the grade of stenosis ($r=0.555$, $p<0.001$) and with calcium score ($r=0.498$, $p=0.001$). 16 participants underwent invasive coronary angiography and in 11 cases at least 1 stent was applied (19 stents collectively applied). 3 out of 11 participants that to date underwent a follow-up CT angiography showed the new onset of coronary plaques, while 1 subject showed progression of pre-existing plaques. Relevant coronary plaques were observed in a large proportion of our study population. Peculiar risk factors such as antiretroviral therapy likely play a role in this process. IMT could represent and easy, adequate and useful tool to evaluate cardiovascular risk in HIV infected subjects. On the other hand, calcium score could underestimate cardiovascular risk in this population due to the high frequency of non-calcified plaques.

STUDY OF THE PREVALENCE OF *ANISAKIS* HYPERSENSITIVITY IN PROFESSIONALLY EXPOSED POPULATIONS

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Background. The workers involved in fish processing can develop allergy to *Anisakis* and a potential occupational risk was suggested. To date, diagnosis of *Anisakis* allergy (AA) is based on the Skin Prick Test (SPT) and specific IgE (sIgE) determination. Anyway, false positivity cases are due to cross reactivity with numerous allergens: *Anisakis* proteins demonstrate considerable immunological cross-reactivity to proteins of related nematodes and other invertebrates such as house-dust mites and cockroaches.

Methods. An observational study was conducted on a target population (fish industry operators, fishermen and cooks) exposed to *Anisakis* allergy risk in Western Sicily. The aim of the study was also to evaluate the reliability of a comprehensive diagnostic algorithm for the AA. A total of 123 subjects were tested by SPT and sIgE for *Anisakis* extracts. Consequently, outpatients who tested positive underwent sIgE testing for Ascaris and tropomyosin. Lastly, patients positive were invited to be tested further by Basophil Activation Test (BAT), as confirmatory analysis. The project is carried out in collaboration with the Buccheri La Ferla Hospital in Palermo (subject recruitment, Skin Prick Test (SPT) and specific dosage of IgE for *Anisakis*, tropomyosin, and BAT). Therefore, the method for extracting the raw *Anisakis* antigen and extracts from excretory-secretory allergens was developed. For BAT test were used both commercial allergenic extracts for *Anisakis* both extracts for *Anisakis* (*A. pegreffii* and *A. simplex* s.s.) prepared at the laboratories of IZS. The allergenic fractions obtained, Anis 1 (20-22 kDa), Anis 4 (9-10 kDa) and the allergen component Anis 5, Anis 8 and Anis 9 (15-18 kDa), were separated by WB electrophoresis.

Results. 6 subjects out of 123 (5%) were positive to SPT and sIgE: 5 were positive to BAT and WB analysis, while a subject employee in the fish industry with clinical signs was positive at the specific IgE determination for *Anisakis*, tropomyosin and *Ascaris* but negative to BAT and WB analysis. A significant difference between basophil activation obtained with *A. pegreffii* extracts and *A. simplex* s. s. extracts was observed with a greater response to the allergens of *A. pegreffii*.

Conclusions. Our findings showed lower positivity cases than what was found in another target population of North-West Sicily. The difference is probably due to a different subjects' recruitment and in particular to the most specific methods used. Our work has been heavily focused on fishing industry operators in which prevention measures are necessary. The partial results obtained in this work support the high clinical specificity of BAT for AA diagnosis, suggesting implementing this method in a comprehensive diagnostic algorithm.

THE EFFECT OF HSV-1 RECURRENT INFECTION ON MODULATION OF AGE-RELATED EPIGENETIC MARKERS

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Background. Herpes Simplex Virus type 1 (HSV-1) is a neurotropic virus capable to establish a latent infection in the host cells and it is known to interact with host epigenetic complexes. The virus genome is chromatinized by the host epigenetic machinery and the viral components are able to counteract the transcriptional silencing induced by the host restriction factors. Growing evidence suggest that viral lifelong infections, together with recurrent/repeated reactivations, can promote the epigenetic imbalance of the host and could affect the cellular homeostasis, but several aspects have yet to be clarified. This topic is intriguing particularly for the role of HSV-1 that has been shown, by our and other groups, as a risk co-factor to Alzheimer's Disease, the main form of dementia in the elderly. To characterize the influence of HSV-1 infections on the host epigenetic balance, particularly in the Central Nervous System, we evaluated the levels of some aging hallmarks, such as post-translational modifications of histones (e.g., H3K56ac), in *in vitro* and *in vivo* experimental models of acute and recurrent virus infection. Moreover, we investigated the expression levels of HIRA and Sin3/HDAC1complex, known to play a crucial role within the epigenetic regulation.

Methods. Primary neuronal cells were obtained by E17 rat embryo brains and infected after 7 days *in vitro* with HSV-1 or MOCK solution, harvested 24h (acute infection) and 8 days post-infection (p.i.) and analysed by Western Blot (WB).
Entorhinal cortex homogenates from HSV-1- and MOCK-infected BALB/c mice were analysed in WB for H3K56 acetylation levels, HIRA and Sin3/HDAC1 protein expression levels. In particular, some mice were analysed 4 days p.i. (acute infection), whereas the others were subjected to several hyperthermia cycles within their life to induce repeated virus reactivations before sacrifice. The virus presence in the brain was tested by PCR and RT-PCR analysis of viral TK gene and ICP4 mRNA and Immunofluorescence analysis of gB expression on brain slices and quantified by virological methods (Standard Plaque Assay, TCID50 and InCell Western Assay).

Results. We found that HSV-1 can modulate the levels of H3K56 acetylation during acute infection and the decrease of H3K56ac was also found 8 days p.i,, suggesting that the virus can promote epigenetic aging *in vitro*. In addition, similar effects were found following recurrent infections in mice, pointing out which complexes could be involved in epigenetic misregulation.

Conclusion. Overall these data strongly suggest that HSV-1 affects cellular epigenetic balance. Further studies are in progress to clarify the mechanism underlying virus-induced epigenetic alterations.

NUCLEAR MAGNETIC RESONANCE BASED-METABOLOMICS ANALYSIS OF URINE IN HCV PATIENTS WITH SEVERE LIVER FIBROSIS RECEIVING DIRECT-ACTING ANTIVIRAL AGENTS

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Background. Hepatitis C Virus (HCV) infection triggers liver inflammation, induces a long term inflammatory response and causes oxidative stress, leading to important modifications of the liver microenvironment characterized by hepatic fibrosis and metabolic alterations. Direct-acting Antiviral Agents (DAAs) induce HCV-clearance but does not completely restore liver dyshomeostasis. Understanding the impact of viral eradication on the liver metabolic activities could allow the optimization of patient's metabolic care during and after HCV cure.

Aim. The aim of the present prospective longitudinal study was to characterize the urinary metabolic profile of HCV-induced severe liver fibrosis and to evaluate the metabolic changes induced by DAAs and HCV clearance by Nuclear Magnetic Resonance (NMR)-based metabolomics.

Methods. The urinary metabolic profile of 23 HCV males with severe liver fibrosis and 20 age-matched healthy-controls was analyzed by NMR-based metabolomics before starting DAAs, at the end-of-therapy, after one and three months of follow-up.

Results. The urinary metabolic profile of patients with severe liver fibrosis was characterized by higher levels of four metabolites related to oxidative stress (pseudouridine, hypoxanthine, methyl-guanidine, dimethylamine) and two amino-acids (glutamine, tyrosine) compared to healthy-controls. N-methyl-nicotinamide, a catabolic intermediate of nicotinamide-adenine-dinucleotide, and 3-hydroxy-3-methylbutyric-acid, an intermediate of leucine catabolism, returned to control levels with viral eradication. Finally, 3-hydroxyisobutyrate and 2,3-dihydroxy-2-methyl-butyrate, intermediates of valine catabolism, increased temporarily during therapy, resulting as potential urinary biomarkers of systemic effects of DAA treatment.

Conclusions. The identified metabolic profiles suggest that oxidative stress persists despite HCV eradication in the context of severe liver fibrosis, suggesting a potential benefit of an antioxidant treatment concurrently with or after DAA therapy. HCV clearance permanently modifies leucine metabolism, while DAA administration temporarily influences valine metabolism, therefore in case of amino-acid supplementation such modifications should be taken into account.

THE HUMAN GTP-ASE RAC 1 PLAYS AN IMPORTANT ROLE IN *PLASMODIUM FALCIPARUM* INFECTION OF HUMAN ERYTHROCYTES

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Background. Malaria is the deadliest parasitosis worldwide, causing 216 milion cases and 445.000 casualities in 2016. The disease is caused by *Plasmodium* parasites that develop and grow inside human erythrocytes. Among them, *Plasmodium falciparum* is the deadliest one. Rac1 is a GTPase known to be involved in infection by several intracellular pathogens, including bacteria, viruses and parasites (e.g. *Toxoplasma gondii*, wich belongs to the same phylum as *P. falciparum*). In this study, we investigated whether Rac1 plays a role also in *P. falciparum* infection of human erythrocytes.

Methods. Rac1 subcellular localization was investigated by Immunofluorescence Assays (IFAs). In order to assess the role of Rac1 in erythrocyte invasion, two different Rac1-KO erythroid cell lines were tested in invasion assays. We also performed invasion assays in the presence of Rac1-specific inhibitors.

Results. During erythrocyte invasion, Rac1 is recruited to the site of parasite entrance in its active state, suggesting that this protein plays a role in the entry process. During the intraerythrocytic growth of the parasite, Rac1 is depleted from erythrocyte membrane to be relocated to the parasitophorous vacuole membrane that surrounds the parasite. To confirm that Rac1 plays a role in *P. falciparum* invasion of the host cell, we generated two Rac1-ko erythroid cell lines and tested them in invasion assays. These experiments showed that the two transgenic lines were both significantly less susceptible to invasion by the parasite, compared to controls. We also tested the effect of Rac1-specific inhibitors on invasion of healthy erythrocytes from donors. These experiments further confirmed the role of Rac1 in the invasion process. Finally, we tested a panel of chemical Rac1 inhibitors on asynchronous cultures and measured the half inhibitory concentrations (IC_{50}). All the compounds reduced parasite growth with an IC_{50} below 20 uM and two among them showed nanomolar IC_{50}.

Conclusions. The GTPase Rac1 plays a role in *P. falciparum* infection of human erythrocytes, both during invasion of the host cell and during the intraerythrocytic growth. Being a well studied protein with a defined X-ray structure and several commercial inhibitors available, Rac1 could be an interesting target for the development of novel anti-

malarial drugs. Drugs targeting the host instead of the parasite have the dual advantage of being less prone to generating drug resistant parasites and to be effective against different parasite strains and possibly different *Plasmodium* species.

TYPE I/II INTERFERON IN HIV-1 INFECTED PATIENTS: EXPRESSION IN GUT MUCOSA AND IN PERIPHERAL BLOOD MONONUCLEAR CELLS AND ITS MODIFICATION UPON PROBIOTIC SUPPLEMENTATION

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Background. A gastrointestinal dysfunction associated with altered microbiome composition and a severe enteropathy characterize the chronic HIV-1 infection, driving persistent immune activation. Recent findings support the ability of probiotics to reverse the gut damage in HIV-1 subjects. Given that type I IFN has detrimental effects during HIV-1 infection and that each IFNα subtypes displays different anti-HIV-1 activity, the expression of all IFNα subtypes, IFNβ and IFNγ was evaluated both in gut-associated lymphoid tissue (GALT) and Peripheral Blood Mononuclear Cells (PBMCs) of antiretroviral therapy (ART) treated HIV-1 patients. Furthermore, the probiotics effects on IFN-mediated immunity were also analyzed.

Methods. Ten HIV-infected subjects with stable suppression of viral load underwent endoscopic procedures and blood collection prior to initiation of probiotics supplementation (T0) and after 6 months (T6). Normal mucosa biopsies were obtained and lamina propria lymphocytes were isolated. Expression of type I and II Interferon (IFN) was measured by RT/ real-time PCR.

Results. IFNα subtypes and IFNβ were expressed at higher levels in GALT compared to PBMC, whereas an opposite trend of expression was recorded for IFNγ. Although a different IFNα subtypes expression pattern was observed in GALT and peripheral blood, some similarities in type I IFN signature have emerged, with IFNα2 and IFNα6/α7, IFNα10, respectively the highest and lowest IFNα subtypes expressed. We also found that IFNα subtypes, IFNβ and IFNγ transcript levels as well as the IFNα subtypes expression profile changed after probiotic supplementation. In particular, IFNα6, IFNα10, IFNα14, IFNα17 and IFNα21 significantly increased after probiotic treatment in both GALT and PBMCs of HIV-1 infected patients. Interestingly, by contrast, IFNγ levels decreased significantly in both anatomical sites after probiotic supplementation.

Conclusions. These findings provide the first evidence that all IFNα subtypes, IFNβ and IFNγ are differentially expressed in the GALT and PBMCs of ART-treated HIV-1 infected patients, and that this multistrain probiotic supplementation can change the expression of some IFNα subtypes and of IFNγ, highlighting the important role of gut microbiome composition in regulating the type I and II IFN response.

EVALUATION OF ANTIMICROBIAL ACTIVITY OF THE ESSENTIAL OIL AND NANO-EMULTIONS FROM *SATUREJA MONTANA*, *L. LAMIACEAE*

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Backgrounds. Essential Oils (EOs) show important antibacterial properties and have been studied as promising sources of novel anti-microbial compounds. A pivotal feature of EOs is hydrophobicity, which damages bacterial membrane, thus interfering with its permeability and causing lysis. EOs of *Satureja* (SEOs) genus are known to have antimicrobial properties. Nano-Emulsions (NEs) are colloidal dispersion in which main components are oil, emulsifying agents and aqueous phases. The aim of this study was to analyze the features of SEOs and NEs and to compare their activity towards several bacterial strains and human cell lines.

Materials and Methods. Compositional analysis of SEOs was evaluated by Gas Chromatography and Mass Spectrometry (GC-MS). Antibacterial activity of SEOs was evaluated against Gram-positive and Gram-negative strains from animal and human samples. Identification and antimicrobial susceptibility tests of bacterial strains were performed by VITEK-2 System. The activity of different concentration of SEOs was measured as MIC and MBC value by microtiter plates broth assay. Bacterial morphological changes induced by oils were revealed by scanning electron microscopy. Oil in Water (O/W) NEs were obtained by sonication of SEO with surfactant, in variable ratio, determining size and properties. Biofilm formation was revealed by crystal violet staining technique. The cytotoxicity was evaluated for SEOs and NEs in cancer cell lines HEp-2 and T24.

Results. Results obtained showed that in SEOs, the prevalent components were carvacrol, cymene, tymol in variable percentages. SEOs possess relevant antibacterial activity demonstrated by MIC and MBC values towards all bacterial strains and a relevant biofilm inhibition in at sub-MIC concentrations. Microbiological results showed that NEs were able to inhibit biofilm production of Gram-negative bacteria. Both SEOs and NEs show cytotoxicity in both cancer cell lines tested.

Conclusions. The results obtained confirm the antimicrobial activity of *S. montana* essential oil, as well as of newly designed nano-emulsions. EOs and NEs could represent a support tool to deal dramatic emergency of the worldwide multi-drug resistance.

Poster session

COMPARISON OF ANTIMICROBIOGRAM IN CYSTIC FIBROSIS POST-LUNG TRANSPLANTATION INFECTIONS AND NON-CYSTIC FIBROSIS POST-LUNG TRANSPLANTATION INFECTIONS FOCUS ON *PSEUDOMONAS AERUGINOSA*

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During the last 40 year Bilateral lung transplantation becomes the basic treatment of End-Stage pulmonary patients, most common diseases which lead to this end-stage situation are: Chronic Obstructive Pulmonary Diseases (COPD), Emphysema, Interstitial Lung Diseases and Cystic fibrosis(CF).

Obviously Lungs Transplantation(LT) has improved the morbidity and mortality in most of those patients, but still the main challenge is the complication after (LT) which are mainly the opportunistic infections, especially that those patient take immunosuppressants to prevent the allograft rejection, and our project focuses on cystic fibrosis (LT) patients' infections compared to non cystic fibrosis (LT) patients , and this classification of non FC (LT) and FC (LT) is very important as they suffer deverse post transplantation infections with a big differences in types, morphology and antibiotics resistance and even the velocity of development of that resistance in the same bacterial type, although both got complete healthy lungs.

Using Microscan Walkaway system for determining the antimicrobiogram for non-fermentative gram- negative bacilli especially pseudomonas aeruginosa the most dangerous bacteria among those patient in relating to respiratory exacerbation and mortality, and non fermentative gram-negative. Also using Antimicrobial Susceptibility Test (AST) VITEK for gram positive especially Staphylococcus aureus the most popular bacteria in those patients, those bacteria are mainly isolated from the culture of sputum, tracheal aspiration, and broncheoalveolar lavage (BAL) fluid with the precise identification of MALDI (Matrix-assisted laser desorption/ionization) TOF Technique.

The importance of this study is confirm that the ability of antibiotic resistance mechanism to survive outside the lungs in a latent state to reinvade the new healthy transplanted lungs which allow then the detection of those latent mechanism and their way of survive in order to prevent them before creating chronic infections in the lungs.

VITAMIN D, SMOKING AND COLORECTAL POLYPS

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Background. Serum vitamin D is mainly produced from the action of sunlight on the skin, (but sun exposure varies among populations) and slightly derived from the diet. Primary role of Vitamin D involves maintaining bone metabolism and calcium homeostasis. It plays an important role in cancer control by reducing angiogenesis and modulating cellular growth. The protective role played by vitamin D on different epithelial tumors has been widely reported. Focusing on the risk of colorectal cancer, vitamin D intake is associated with a reduced risk of colorectal cancer. Smoking is a risk factor for colon cancer, but little is known about the effect of smoking on Vitamin D.

Aims. This study aims to evaluate the role of smoking and Vitamin D levels in patients with colorectal polyps and without it in Saudi people.

Methods. Some patients undergoing a colonscopy at King Abdulaziz Hospital and King Khalid Hospital will be enrolled in the study. Ethics approval will be obtained. Inclusion and exclusion criteria will be collected using a questionnaire. Questions about Vitamin D: questions will be aimed to register the amount of Vitamin D and to investigate lifestyle characteristics. Questions about Smoking: questions will be aimed to investigate when smoking started, nicotine dependence type of smoking. Questions about colorectal polyps: information will be collected from clinical records.

Eventual results. Vitamin D metabolism has been established to be modulated .but the interactions with smoking has not been well studied. This study aims to investigate this aspect and an expected result is to find an inverse association between smoking and vitamin D level; heavy smoking and low level of Vitamin D are expected to increase colorectal cancer risk similarly to what found by the HUNT study in the respiratory context. Vitamin D level, smoking and lung function in adults showed that associations among never-smokers were null whereas significant associations were observed in ever-smokers. A research approach will be adopted. Dietary and lifestyle data will be gathered.

Conclusions and prospective. This study evaluates the role of interaction between the topics. If expected results are confirmed, quitting smoking and optimal level of vitamin D should be recommended to avoid risk of colorectal cancer. Additionally, other factors, such as skin exposure to the sun, could be explored and investigated among different populations to determine whether population-specific characteristics may influence study results.

ACUTE SPINAL CORD INJURY: FROM BEDSIDE AND DISSECTING TABLE TO BENCHSIDE, UNTIL INVESTIGATING MIRNA FAMILIES INVOLVED

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Background. Spinal Cord Injury (SCI) consists of a plethora of signs and symptoms resulting from a combination of different factors among which the primary impact, the subsequent cellular swelling, the continuous spinal cord compression, vascular (linked to the integrity of the arterial feeding and of the venous outflow) and intrinsic cellular mechanisms. In recent years there has been a progressive epidemiological increase and a trend reversal linked to a greater number of incidences in elderly people of a pathology historically linked to young age. Acute traumatic SCI involves primary and secondary injury mechanisms. The primary mechanism is related to the initial traumatic damage caused by the damaging impact and this damage is irreversible. Secondary mechanisms, which begin as early as a few hours after the initial trauma, include processes such as spinal cord ischemia, cellular excitotoxicity, ionic dysregulation, and free-radical mediated peroxidation.

Methods. The purpose of the work is dedicated to provide a concise review in a rapidly evolving field such as SCI, featured by different forms of injury, investigating the pathology and degree of clinical diagnosis and treatment strategies, the animals models that have allowed us to better understand this entity and, finally, the role of new diagnostic and prognostic tools such as miRNA and the perspectives on the future of research about SCI. Many authors claimed miRs to be potential new targets for the treatment of SCI. Since miRNAs can regulate many genes at the post-transcriptional level, they are attractive candidates as upstream regulators of the secondary SCI progression.

Results. SCI is featured by different forms of injury, investigating the pathology and degree of clinical diagnosis and treatment strategies, the animals models that have allowed us to better understand this entity and, finally, the role of new diagnostic and prognostic tools such as miRNA could improve our ability to manage this pathological entity. Autopsy could benefit from improvements in miRNA research: the specificity and sensitivity of miRNAs could help physicians in determining the cause of death, besides the time of death. For all the above mentioned reasons, miRNAs could become in the next future reliable forensic biomarkers for the diagnosis and prognosis of SCI.

Conclusions. In conclusion, the miRNAs involved in the SCI-related pathways, which were discussed earlier in the review, could become part of the routinary clinical practice integrating current histological and immunohistochemical investigations.

EXTRACELLULAR VOLUME FRACTION BY QUANTITATIVE DYNAMIC EQUILIBRIUM CT PROVIDES INSIGHTS INTO ACUTE, CHRONIC AND SUB-CLINICAL PATHOLOGY INFLAMMATION

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Background. Inflammation in response to infection and injury is a critical survival mechanism used by all higher vertebrates. Chronic inflammatory conditions are associated with the prolonged release of inflammatory mediators and the activation of harmful signal transduction pathways, all of which contribute disease development and phenotypes. Quantitative Dynamic Equilibrium CT (DynEQ-CT) of Extracellular Volume Fraction (ECV) may be able to detect subtle abnormalities such as diffuse inflammation acute or chronic due to infection and/or fibrosis. The validity of this technique was preliminarily evaluated in a study with 20 patients suspected to have diffuse inflammation in the myocardial tissue. Using HU (Hounsfield Unit) values before and after administration of an Extracellular Contrast Agent (ECA) allows the additional calculation of the ECV, well established in CT. In fact, the ratio of the change in blood and tissue attenuation (ΔHU) represents the contrast agent partition coefficient. If the blood volume of distribution is substituted in (1-hematocrit), ECV=(1-hematocrit)×(ΔHUtissue/ΔHUblood).

Objectives. The project will focus to measure ECV in different tissues of patient with acute and or chronic infections before and after specific.

Preliminary results. Pre-contrast HU were significantly longer in patients with myocarditis compared with control group (1125.2±42.1 *vs* 1073.2±33.1, p<0.011). ECV was significantly higher in patients with myocarditis compared with controls (33±3.1% *vs* 27.7±3.2%, p=0.012). Preliminary analysis indicates quantitative DynEQ-CT parameters (HU: r=0.76, p=0.012; ECV: r=0.811, p=0.021) with strong correlations with inflammation of the heart muscle, especially with ECV. Stratification of severe tissue structure was well discriminated by ECV quantification. The ECA remains strictly extracellular and does not enter parenchymal or non-parenchymal cells. Therefore, ECV strictly mirrors the volume of the deposited extracellular matrix.

Conclusions and perspectives. We hypothesized that quantitative assessment of tissue ECV would be clinically useful for detecting both focal and diffuse tissue abnormalities in a variety of acute and chronic infectious conditions. ECV imaging can quantitatively characterize tissue inflammation, atypical diffuse fibrosis, and subtle tissue abnormalities not clinically apparent on different method images. Therefore, ECV not only can detect tissue inflammation and/or fibrosis but also might quantify response to treatment during follow-up.

EVALUATION OF IGG ANTIBODY RESPONSE TO *AEDES* SALIVARY PROTEINS: FIRST ATTEMPT TO VALIDATE SEROLOGICAL MARKERS OF EXPOSURE IN A MURINE MODEL

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Background. The rapid spread in the European continent of *Aedes albopictus* and its involvement in recent outbreaks of chikungunya and dengue in Italy, France and Croatia highlighted the need to improve surveillance and control of *Ae. albopictus* and other *Aedes* invasive species. Previous studies showed that the IgG response to the *Anopheles gambiae* salivary protein gSG6 is a reliable marker to evaluate human exposure to malaria vectors. The present study aim to develop similar serological tools to assess host exposure to *Aedes* mosquitoes using *Aedes*-specific salivary proteins already identified by comparative analyses.

Materials and Methods. Three groups of naïve BALB/c mice were exposed to bites of *Ae. albopictus*, *Ae. aegypti* and *An. coluzzii*. Serum samples were collected before exposure, after the 2nd and the 4th/last exposure and then 1, 2, 3, 5 months later. The IgG response to salivary gland extracts (SGEs), to the alb1 salivary protein from *Ae. albopictus* and to its ortholog from *Ae. aegypti* (aeg1) was measured by ELISA. We also measured the response in a volunteer who regularly fed an *Ae. albopictus* colony for ~3 months (L13) and then after 2 years of non-exposure (L16).

Results and conclusions. The immunization protocol was effective, especially for *Ae. albopictus* and *Ae. aegypti*, as indicated by the IgG response to SGEs. Two of the four *Ae. albopictus*-exposed mice had IgG antibodies against alb1 but no one responded to aeg1. All *Ae. aegypti*-exposed mice exhibited high levels of anti-aeg1 IgG but no antibodies to alb1, confirming that there was no significant immune cross-reactivity in mice. Similar results were found in the single human hyperimmune serum (L13) analyzed, with high levels of anti-alb1 IgG and a negligible response to ae1. Further validation, making use of a larger and proper set of human sera from individuals naturally exposed to *Ae. albopictus*, is on going.

TOXICOLOGICAL EVIDENCES AND MECHANISMS OF DAMAGES FOLLOWING CAFFEINE CONSUMPTION IN PROFESSIONAL AND AMATEUR ATHLETES AND CADAVER

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Background. Caffeine is the most widely consumed psychoactive compound worldwide. It is mostly found in coffee, tea, energizing drinks and in some drugs. However, it has become really easy to obtain pure caffeine (powder or tablets) on the Internet markets. Mechanisms of action are dose-dependent. Serious toxicities such as seizure and cardiac arrhythmias, seen with caffeine plasma concentrations of 15 mg/L or higher, have caused poisoning or, rarely, death; otherwise concentrations of 3-6 mg/kg are considered safe. Caffeine concentrations of 80-100 mg/L are considered lethal. Although caffeine intoxication is relatively uncommon, raising awareness about its toxicological consequences could be useful for both clinicians and pathologists to identify possible unrecognized cases and prevent related severe health conditions and deaths. The use of caffeine among athletes is widely reported, and its use is frequent because of the believed effects on physical performances. Our project aims to determine differences, if any, in caffeine levels encountered in blood samples obtained from professional athletes, non-professional athletes and cadavers (representative of the general population).

Methods. We proceeded with the enrollment of athletes of different disciplines on a voluntary basis and out of completion; so that, caffeine consumption and eventually use of other substances will be representative of a normal and habitual consumption. Similarly, cadavers (aged < 50 years-old) came from morgues of the center of Italy.

Results. Thank to our study we would like to demonstrate that caffeine levels in professional and non-professional athletes will be higher than in general population; one of the reason of this belief is that caffeine is not considered a performance-enhancing substance (doping agent) in the sportive community. Moreover, given the well-known co-assumption of caffeine with other psychoactive substances (e.g., steroids and cocaine), we suppose that other substances than caffeine will be present in athlete's toxicological samples.

Conclusion. Results of our study may help to better understand the magnitude of caffeine use and abuse among professional and amateur athletes and to support clinicians and pathologists to prevent serious health consequences related to the consumption of this substance.

APPLICATION OF EFFECT-BASED METHODS FOR THE MONITORING OF TIBER RIVER BASIN

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Background. The use of effect-based methods for the assessment of the quality status of surface waterbodies has been highlighted and recommended in the context of the Common Implementation Strategy of the Water Framework Directive in particular for the detection of complex chemical mixtures and emerging contaminants; these methods (bioassays *in vitro* and *in vivo*, biomarkers) can be used, together with chemical monitoring, for the role of screening or early warning systems. Furthermore the effects of climate changes (e.g. water scarcity, flooding) can modify the environmental fate of several contaminants in the ecosystems and the use of effect-based methods is recommended because they can detect a signal of the deterioration of the status of the waterbodies.

Methods. In this research effect-based methods have been applied in the urban part (Rome) of the Tiber river basin in order to evaluate the chemical quality and the presence of possible synergic effects caused by mixtures of pollutants. The Tiber river basin is characterized by several sources of pollution that include, *inter alia*, urban waste water effluents, illegal landfills, diffuse pollution linked to agriculture, small enterprises discharges, plastics; these sources of pollution can release in the Tiber river several contaminants that can include also pharmaceuticals, personal care products, solvents, metals and several other organic contaminants. The effect-based methods used in the project have included the Fish Embryo Toxicity Test with the detection of lethal and sub-lethal effects, the acute assay with Daphnia Magna and the algae test. The monitoring campaigns are conducted in different seasons of the year in 3 sampling stations including a potential background area and a station located in the urban trait of Aniene river.

Results. The preliminary results of the first monitoring campaign have showed the presence of ecotoxicological effects, with different gradients, in all the sites analyzed included the background area, but for a robust scientific assessment and interpretation about the quality status of the river it is necessary to wait for the results of the future monitoring campaigns foreseen in the project.

Conclusions. The results of this study, will contribute: 1) to improve the knowledge of the chemical quality status of the urban part of the Tiber River basin 2) to define a set of effect-based methods needed to support the implementation of the national and European legislation.

RISK MAPPING IN THYROID SURGERY: MEDICO-LEGAL MANAGEMENT OF A RECURRENT ISSUE

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Background. Thyroid surgery represents a particular field due to the potential post-operative complications that sometimes have a significant impact on patients' quality of life. Such a type of surgery involves significant risk of bleeding, airways impairment, nerve injury, vocal cord paralysis and death. The aim of the present study is to review thyroid related surgery litigation in order to identify pitfalls and propose possible strategies for reducing claims.

Methods. The study was conducted on thyroid surgery related claims occurred at Umberto I General Hospital in Rome from 2007 to 2018. Data related to the claims recorded in the study period were collected at Hospital's Legal Affairs Office. All claims were classified according to gender and age of the patient, type of event, patient outcome, date of the event, complaint date, amounts requested and amounts paid. The definitions of disputed events were elaborated matching Diagnosis Related Groups (DRGs) with the types of event codified in the International Classification for Patient Safety (ICPS) system. Finally, a descriptive statistical analysis of categorical variables with the representation of frequencies in absolute terms and in percentage was performed.

Results. During the study period, 47 claims, mostly managed through a self-insurance plan, were reported. The sample under study was predominantly composed of female patients (45:2). As regard the type of event, thyroid surgery related claims were classifiable as “clinical process and procedure” (44; 94%), “blood and blood products” (2; 4%) and “organizational management problems” (1; 2%). In the context of procedural inadequacies, the adverse events identified were recurrent laryngeal nerve injuries (31; 70%), incomplete removal of the thyroid (6; 14%), incongruous removal of the parathyroid glands (4; 9%), development of keloid scars (2; 5%), and dental avulsion due to airways maneuvers during anesthesia (1; 2%). Nowadays, out of the 47 total claims, 32 (68%) are still open, 8 (17%) were liquidated and 7 (15%) were rejected. The overall economic impact was € 261,883 with an average amount of € 32,735 per claim.

Conclusion. The obtained results demonstrate that the methodological assessment of the litigation allows identifying critical points in the care pathways and planning risk management measures able to increase treatment standards and reduce litigation.

PATIENT ACTIVE INVOLVEMENT IN RESEARCH: THE ROLE OF CYSTIC FIBROSIS PATIENTS ORGANIZATIONS IN EUROPE

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Patient active involvement in research ("experimenting with" as opposed to "experimenting on" patients) makes research more accountable and transparent, leads to better results and generates research that is more relevant to patients. The Patient-Centered Outcomes Research Institute in the USA and the James Lind Alliance in Europe have outlined the differences in research priorities between doctors and patients and instituted measures to ensure that patients participate in the whole research process. In Italy, the Cystic Fibrosis Patient Centered Outcomes Research Group (IPaCOR-CF) described a research prioritization effort that involved 180 trained and untrained stakeholders (SH), showing the need to consider the education level and the delivery of ad hoc training activities by professionals to broaden the base of patients and SH who may be considered qualified to transfer the PCORI principles into practice. Therefore, it appears crucial that Cystic Fibrosis (CF) Patients Organizations in Europe organize initiatives aimed at defining research strategies that involve patients' and relatives' needs.

The overall purpose of this study, patient's empowerment in CF, passes through the definition of research strategies that involve patients and SH and consider their real needs. This objective, in turn, needs strengthened knowledge of the research methodology by the stakeholders, having at the horizon the perspective to use the acquired methodology to promote the development of future studies and to the disseminate the best practices, processes, and methods for patient involvement in research generation in Europe. To do this, a survey was conducted among the European Patients' Organizations (POs) to investigate which roles they are playing to promote patient engagement in research, in order to get an overview of the different PO-initiated actions for patient engagement already existing throughout Europe and to learn how to better integrate patients' needs in scientific projects.

The survey was sent to 39 POs in Europe. In the first submission, 28 surveys were returned (72% response rate). Patients active involvement in all phases of the research process is considered an important issue among POs. The resources used are many, but not evenly distributed across Europe. There is a diffuse need to train the "expert patient", who can proactively collaborate with companies, researchers, governments, registers, untrained patients and other SH to promote a research based also on patients' needs.

GLIA-NEURON CROSSTALK DURING HSV-1 INFECTION AND ITS ROLE IN NEURONAL DAMAGE

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Introduction. Herpes Simplex Virus type 1 (HSV-1) establishes a lifelong infection in the peripheral ganglia and, following periodic reactivation, may reach the Central Nervous System (CNS) where its replication has been associated to induction of neurodegenerative processes typical of Alzheimer's Disease (AD). Previous data show that *in vitro* HSV-1 infection enhances neuronal appearance of AD hallmarks: production/accumulation of neurotoxic fragments of Amyloid Precursor Proteins (APP) and hyperphosphorylation of Tau protein; this data were recently confirmed in an *in vivo* recurrent HSV-1 infection model. It is known that CNS is populated not only by neurons, but also by glia and microglia and it is possible to hypothesize that, during HSV-1 infection, these cells surrounding neurons may undergo activation and expression of proinflammatory genes, enhancing neuronal damage.

Aim. To investigate the glia-neuron crosstalk during HSV-1 infection and its role in neuronal damage.

Methods. Primary cultures of neuronal and glial cells were obtained by E17 rat or mouse embryo brains. Human and mouse neuroblastoma (SH-SY5Y and Neuro2A, respectively), human glioblastoma (A172) and mouse microglia (BV2) cells were grown in Dulbecco's modified Eagle's medium containing 10% heat-inactivated FBS and antibiotics (glutamine 0.3 mg/ml, penicillin 100 units/ml, streptomycin 100 μg/ml). Confluent cellular monolayers were infected with HSV-1 (strain F) at m.o.i. 1 for 18 hours and analyzed by Western Blot to detect tau phosphorylation and APP fragmentation. HSV-1 titers were measured in conditioned media by standard plaque assay. Cytokines and chemokines production were evaluated by ELISA. Amyloid beta peptides production was investigated by confocal Microscopy assay.

Results. We have set up four HSV-1-infected neurons–glia co-culture models: human neuroblastoma/glioblastoma, mouse neuroblastoma/microglia, primary rat neurons/astrocytes/microglia, primary mouse neurons/astrocytes/microglia. In these models we found that the presence of glial cells increases Tau phosphorylation (particularly at Thr 205 residue), beta - amyloidogenic APP cleavage, pro-inflammatory cytokine (IL-6) and chemokines (CCL5 and CCL2) production in HSV-1 infected neurons–glia co-cultures compared to infection of single cultures. Further studies are in progress to clarify the mechanisms underlying the influence of glial cells on Alzheimer's disease hallmarks appearance during HSV-1 infection.

HEALTH IMPACT OF DIRECT ANTIVIRAL AGENTS AGAINST HCV (HI-DAA)

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Background. In 1990 HCV was recognized as the cause of Chorionic Hepatitis C (CHC). CHC is associated with several hepatic and extrahepatic condition. Since 2014, Direct Antiviral Agents (DAAs) have been approved for treatment of CHC. DAAs have shown to be able to eradicate HCV infection in most of the patients however little is known on the effect of viral eradication on established hepatic and extra hepatic damage. The Health Impact of Direct Antiviral Agents (HI-DAA) study has the aim of assessing the effect of HCV eradication on established damage including glucose metabolic impairment, liver fibrosis and liver carcinogenesis. The study has been funded by Italian Ministry of health in 2018 (GR-2016-02363036). Here we present a preliminary analysis on data on metabolic impairment recovery in subject who cleared HCV infection with severe liver fibrosis.

Methods. The study analyzed a historical cohort study of patients with CHC and established severe liver damage including Metavir stage F3 fibrosis and cirrhosis who eradicate viral infection after therapy with DAA. As marker for viral eradication was used the sustained virologic response at 12 weeks after the endo of therapy (SVR12). The analysis was carried out on repeated measures of glycemia through a multilevel regression model with random intercept at the level of patients and random slope at the level of time after start of therapy with DAA.

Findings. The study included 205 patients who achieved SVR12 at INMI Lazzaro Spallanzani liver Unit in Rome (Italy) between March 2015 and October 2016. Analysis for assessing temporal trend of glycemia and variation of glycemia according to HCV viral load suggested that that blood glucose levels significantly dropped, in patients with diabetes. Indeed, a significant reduction of glycemia levels occurred between week 3 and 5 therapy in temporal coincidence with HCV clearance ($p<0.001$). In contrast in normoglycemic patients only non-statistically significant blood glucose variations were observed.

Interpretation. Our study provides evidence that DAAs therapy may reduce glucose metabolic impairment of patients who eradicate HCV infection with already established severe liver damage.

IMMUNIZATION POLICIES AND PRACTICES TARGETING NEW ARRIVING MIGRANTS

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Background. Migrants represent a potential vulnerable group and adequate health assistance, including vaccine preventable diseases prevention, should be ensured. Indeed, migrants are included in the EVAP (European Vaccine Action Plan 2015-2020) in order to ensure them vaccinations and information about vaccinations. The Istituto Superiore di Sanità launched a survey with the aim of investigating immunization policies targeting migrants in EU/EEA countries.

Methods. The web-based cross-sectional survey was conducted in 28 EU and 2 EEA (Iceland, Norway) countries within the ECDC (European Center for Disease Prevention and Control) funded Vaccine European New Integrated Collaboration Effort (VENICE) Project. Data were collected in the period January-April 2018.

Results. All countries but the Czech Republic completed the survey and 28 countries (all except Romania) offer vaccination to migrants. A national regulation/legal framework supporting migrant immunization is available in 24/28 countries. All the vaccinations included in the National Immunization Plan appropriate for age are offered to child and adolescent migrants in 27 countries and to adult migrants in 13 countries. Priority is given to polio, dT/dTP and MMR vaccines. The use of laboratory evidence of immunity in case of unknown or uncertain immunization status is requested for child/adolescent and adult migrants, respectively, in 3 and 4 countries. Vaccinations are mainly given at holding and/or community level and only 5 countries vaccinate at entry level.

Conclusions. The results show that policies regarding migrants' immunization are available in most of EU /EEA countries, generally in line with WHO and ECDC recommendations. In fact child and adolescent migrants are mainly offered all the vaccination as to country national immunization plans, even in case of undocumented or uncertain immunization status. In this case, ECDC recommends to consider migrants as unvaccinated and to vaccinate them according to national immunization plans (offering to children/adolescents at least vaccinations against MMR, dTp, polio and HiB, and to adults at least vaccinations for MMR, dT and polio). Also data about site of vaccinations delivery are in line with WHO-UNHCR-UNICEF joint statement recommendation that suggests not to offer vaccinations at entry point, unless there is an outbreak of VPDs in the hosting or transit country. In these cases, migrants should be included in all programs of VPDs control. Concluding, mapping out national health policies and differences across countries is a strategic resource to improve migrant health.

EVALUATION OF PATIENT SAFETY IN ITALY: THE NATIONAL OBSERVATORY

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According to the OECD high-quality national healthcare service should provide safe, effective and patient-centred care. In Italy, in 2017 a national legislation on patient safety instituted the National Observatory for patient safety. The Observatory is a network participated by Italian national institutions (Agenas, AIFA, CSS, ISS, Ministry of Health), regional health authorities, and national experts with the aim of monitoring the Adverse Events (AEs), near misses and the main risks associated with healthcare provision and providing national guidance to improve patient safety.

The first project undertaken by the Observatory was the creation of a national monitoring system for patient safety. This project contemplates three phases: adoption of a theoretical framework, data/information sources review and elaboration of data sources catalogue, and indicators selection and calculation.

The theoretical framework, inspired by the one realized by OECD for healthcare quality evaluation, takes into account on one side the patients' needs (primary prevention, getting better, living with illness or disability/chronic care, coping with end of life) and on the other side the main priorities for patient safety (governance, healthcare-acquired infections, antimicrobial-resistance, surgery and surgical procedures, medication safety, transfusions and transplants).

Once the theoretical framework was defined, we investigated the availability of data useful for safety evaluation at a national level. Several authors at international level focus on the relevance of utilising more than one data source to identify AEs and risks associated with healthcare. Kaveh Shojania in the paper "The Elephant of Patient Safety" compares patient safety to a big elephant which cannot be even identified as an elephant if it is seen from a single, close point of view. Integration of multiple and different points of view may allow a full description of the elephant of patient safety. With this aim, we performed a recognition of all data sources available at a national level potentially useful to monitoring patient safety. We identified a total of 29 national data sources.

Based on the theoretical framework and on the data sources catalogue we selected the indicators according to four criteria: relevance, comparability, feasibility, and actionability. Totally 19 indicators were selected and calculated for the area of governance, 40 healthcare-acquired infections and antimicrobial resistance, 23 for surgery and surgical procedures, 32 for the medication safety and 8 for transfusions. Indicators were calculated for the regional level utilising 14 out of 29 data sources collected in the catalogue.

AEROSOLIZED BOVINE LACTOFERRIN COUNTERACTS INFECTION, INFLAMMATION AND IRON DYSBALANCE IN A CYSTIC FIBROSIS MOUSE MODEL OF *PSEUDOMONAS AERUGINOSA* CHRONIC LUNG INFECTION

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Background. Cystic Fibrosis (CF) is a genetic disorder affecting several organs and reducing expectancy and quality of life. The most relevant damages are observed in the airways that are inherently prone to infection. The chronic airway infections in CF patients are often sustained by *Pseudomonas aeruginosa*. Airways inflammation is a hallmark of CF, being present even before bacterial colonization but it is exacerbated after infection. In addition to infection and inflammation, a dysbalance of iron homeostasis is observed in CF airways and high levels of iron (up to >100 μM) in airway secretions can be recorded. Iron excess can derive from the altered expression of the main proteins involved in iron homeostasis. In particular, an increased expression of both Ferroportin (Fpn), the sole mammalian iron exporter, and Ferritin (Ftn), the main iron storage protein, in lung tissue of CF patients has been observed. Moreover, elevated concentrations of Transferrin (Tf), the main iron transport protein in blood, in the lung lavage of CF patients were found. The aim of this study was to investigate the effect of bovine Lactoferrin (bLf), a multifunctional iron-chelating glycoprotein of innate immunity, in a CF murine model of *P. aeruginosa* lung chronic infection.

Methods. To induce lung chronic infection, C57BL/6 mice, either CFTR-deficient or wild-type, were intra-tracheally inoculated with agar beads suspension containing *P. aeruginosa* MDR-RP73 strain to mimic biofilm lifestyle. Treatments with aerosolized bLf (200μg/50 μl of freshly prepared solution) or saline were started soon after infection and repeated daily for six days. After quantification of total protein content with Bradford's assay, cytokine levels in supernatants of lung homogenates were analyzed using the Bio-Plex Protein Array System while pellets of lung were used for western blot analysis for Fpn, Ftn, Tf Receptor 1. In addition, bronchoalveolar lavage fluid was used for iron quantification.

Results. Our results demonstrated that aerosolized bLf was effective in significantly reducing both pulmonary bacterial load and infiltrated leukocytes in infected CF mice. Furthermore, for the first time, we showed that bLf reduced pulmonary iron overload, in both infected WT and CF mice. In particular, at molecular level, a decrease of both the iron exporter ferroportin and iron storage ferritin as well as of luminal iron content was observed.

Conclusion. Overall, bLf acts as a potent multi-targeting agent able to break the vicious cycle induced by *P. aeruginosa*, inflammation and iron dysbalance, thus mitigating the severity of CF-related pathology and sequelae.

THE DEVELOPMENT OF STRATEGIES TO CONTRAST VACCINE HESITANCY IN ITALY

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Background. The extension of compulsory vaccination, introduced by law in 2017 in Italy, may not be sufficient to guarantee the compliance with immunization coverage in the long term. The aim of this research project is to assess knowledge and attitudes on vaccinations and on mandatory immunization in different populations (pregnant women, midwives, public health professionals), in order to support the development of tailored strategies to contrast vaccine hesitancy in the Country.

Methods. We conducted a cross-sectional survey on a sample of pregnant women attending antenatal classes (CANs) in Rome through distribution of a self-administered questionnaire. Multiple logistic regression models were built to analyze the determinants of knowledge, attitudes and intention to vaccinate in this population. An online survey to identify level and determinants of knowledge and attitudes about vaccinations of midwives members of the professional register of Rome is currently ongoing, while a survey aimed at addressing the attitudes of Italian Public Health (PH) professionals on mandatory vaccinations is under development.

Results. A total of 458 pregnant women attending CANs in 36 family health centers and two hospitals in Rome answered the survey. More than 26% of respondents showed a good level of knowledge of the safety and efficacy of vaccines, but there were high rates of uncertainty or agreement with some of the most common anti-vaccination thesis. Only 75% of women were sure about vaccinating their children with the hexavalent vaccine, and 64.3% with MMR. A good level of knowledge was the strongest predictor of positive attitudes towards vaccination (OR 11.61, 95% CI 6.43-20.96), which, in turn, influenced the intention to vaccinate for most vaccines, together with the perception of the benefit of immunization. Preliminary results on data collected from 87 midwives show a heterogeneous level of knowledge in this population: only 62% respondents were certain of the safety of multiple shots at the same time, while 24% agreed that three-month-old children are too young to begin the immunization schedule.

Conclusions. Scepticism about the safety, efficacy and importance of vaccines is associated to pregnant women's hesitancy on vaccinations, suggesting the need to develop strategies to increase vaccine acceptance in the antenatal period. Based on the results of the two surveys, we will focus on increasing the capacity of HCWs working in the antenatal setting, particularly midwives and nurses, to correctly deliver information to future parents. The results of the survey addressed at PH professionals will allow evaluating the impact of the mandatory vaccination policy on the PH services in the Country.

E-LEARNING COURSES AT ITALIAN NATIONAL INSTITUTE OF HEALTH: CHARACTERISTIC OF DROPOUT PARTECIPANTS

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Background. Over the last decades, the number of adult learners who participate in e-learning, has rapidly grown, due to its flexibility. In Italy, health professionals in active clinical practice, are required to keep their knowledge up to date, through continuing medical education scheme. At annual basis, they have to provide 50 credits (25 minimum and 75 maximum) or 150 triennially. Since 2004, the Training Office of the Italian National Institute of Health (ISS), provides Continuing Medical Education (CME) e-learning courses in public health, using Problem Based Learning (PBL) methodology.

The aim of this study, was to identify and describe the magnitude and characteristic of dropout participants in e-learning courses delivered during the 2017-2019 CME triennial.

Further analysis will be directed to understand factors that underline the dropout rate and consequently, hypothesize actions to improve completion rates.

Methods. Data on participants of e-learning courses delivered in the last three years are analysed. A series of variables are used to characterize the different types of courses: low, medium, high interaction, open to all professions CME and non CME. Participants are classified as completers who passed (>75%) the final certification test. While dropouts, are classified as early leaving, lurker and abandonment, according to the level of completion of the course. Descriptive and inferential analysis are performed through SPSS software.

Results. A total of 20 courses (n=41.948 participants) delivered between january 2017 to may 2019, were analysed. These courses were distributed in 7 medium and 13 low interactive models, all accredited CME and covering a wide range of health professionals, medical and non-medical, through invitation and self-enrolment modality. The workload varied between courses, of which 4 predicted 48 hours and 10 courses predicted 16 hours and the rest distributed between 12, 20 and 30 hours respectively. Overall, data show completion rate of 68%, dropout rate of 30% and not passed rate about 2%, with a great variability based on the type of course and level of interaction.

Conclusions. Based on these findings, we intend to conduct further study to explore in-depth determinants of dropout from ISS e-learning courses.

CARBAPENEM-RESISTANT *KLEBSIELLA PNEUMONIAE* INFECTIONS IN A COHORT OF POLYTRAUMA PATIENTS IN THE INTENSIVE CARE UNIT

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Background. The impact of infections caused by carbapenem-resistant Gram-negative bacteria, especially *Klebsiella pneumoniae*, on morbidity and mortality of patients suffering from multiple injuries, and admitted to the Intensive Care Unit (ICU), is not clearly established. We did a prospective observational study to characterize the epidemiology and outcomes of infections and colonization by KPC-producing *K. pneumoniae* among polytraumatized patients in ICU.

Methods. We recruited patients from those referred to the ICU because of multiple injuries, from November 2017. The severity of polytrauma was determined with the Injury Severity Score (ISS). The colonization and resistance dynamics of bacteria were investigated during hospitalization, and infections according to CDC/NHSN criteria were recorded.

Results. A total of 52 patients were enrolled in the study: 40 males (77%) and 12 females (23%); the median age was 33 years (range 18-83 years), and the median ISS was 34 (range 17-54). The median length of stay in the ICU was 29 days (range 3-173 days), and the overall mortality at 30 days was 15,5%. During the observation period, the majority of patients (61.5%) experienced at least one infection. KPC-producing *K. pneumoniae* was detected in 22 patients (42%). In 77% of cases, the detection of carbapenem-resistant *K. pneumoniae* was associated with an infection, mainly sepsis, whereas in the remaining cases there was only a colonization.

Conclusions. Our study showed that polytrauma is not an independent risk factor for infection/colonization by KPC-producing *K. pneumoniae*. Mortality rate in the subgroup of patients infected or colonized by this microorganism doesn't differ from the mortality rate among other groups of critically ill people, but the length of stay is significantly longer in the former group ($p=0.005$). We didn't find differences in terms of age, gender, ISS between patients colonized or infected by KPC-producing *K. pneumoniae* and patients without infections or with infections caused by other microbes ($p>0.05$).

A FAST UHPLC-MS/MS METHOD FOR THE DETECTION OF FENTANYL ANALOGUES AND METABOLITES IN CONVENTIONAL AND NON CONVENTIONAL BIOLOGICAL MATRICES

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Introduction. A severe increase in overdose fatalities involving synthetic opioids, as fentanyl and its analogues illicitly manufactured has been recently worldwide observed becoming a growing threat for public health. The rapid coming out of these substances into the illicit market renders more difficult their identification. Thus, a regular updating of the analytical methods is required to keep up with this rapidly evolving market. The aim of this project was the development and validation of an UHPLC-MS/MS method for the rapid and sensitive detection of the newest fentanyl analogues in whole blood, urine and hair.

Methods. UHPLC-MS/MS analysis was performed on a Waters® Xevo® TQ-S micro mass spectrometer equipped with an electrospray ionization source in positive ion mode and interfaced with an ACQUITY UPLC® I-Class. Separation was performed on an ACQUITY UPLC® BEH C18 column (50 mm x 2.1 mm, particle size: 1.7 µm). Run time was 8 min (gradient mobile phase: 0.1% formic acid in 5 mM ammonium acetate buffer (A) and 0.05% formic acid in acetonitrile (B); flow rate of 0.35 mL/min). ESI+ conditions: capillary voltage = 0.5 kV, source t. = 150°C, desolvation t. = 650°C, cone gas flow rate = 20 L/h, desolvation gas flow rate = 1,200 L/h. The validated method was then applied to 42 post-mortem biological specimens collected after deaths involving fentanyl analogues. Urine specimens were diluted and directly injected into the UHPLC-MS/MS system without any sample pretreatment; for blood testing a liquid-liquid extraction (LLE) was performed and a solid phase extraction (SPE) was carried out for hair samples.

Results. Cyclopropylfentanyl, cyclopropyl norfentanyl, methoxyacetylfentanyl, acetylfentanyl, acetyl norfentanyl, fentanyl, norfentanyl, furanylfentanyl, furanyl norfentanyl and 4-ANPP (despropionylfentanyl) were detected in blood and urine in a high number of cases. In hair specimens fentanyl, norfentanyl and 4-ANPP were found at elevated concentrations in 4 cases.

Conclusion. The obtained results showed that cyclopropylfentanyl was the most prevalent analogue detected in the analyzed matrices; acetylfentanyl, fentanyl, furanylfentanyl, methoxyacetylfentanyl, sufentanil and metabolites were also found. Cyclopropyl norfentanyl was a good marker of cyclopropylfentanyl consumption, whereas methoxyacetyl norfentanyl and furanyl norfentanyl were not suitable markers of methoxyacetylfentanyl and furanylfentanyl intake, respectively. Although 4-ANPP is a metabolite of several other fentanyl analogues it may be a good biomarker for furanylfentanyl consumption. Further studies will be developed to improve the analytical method in other biological matrices and to identify other fentanyl analogues.

PREVENTION OF MOTHER-TO-CHILD TRANSMISSION OF HIV IN THREE DIFFERENT REGIONS OF CAMEROON: DETERMINANTS AND BARRIERS AFFECTING MOTHER-CHILD HEALTH IN LIMITED RESOURCE SETTINGS

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Background. Mother-To-Child Transmission (MTCT) of HIV remains a major global public health burden in sub-Saharan Africa, despite mother-child Antiretroviral (ARV) prophylaxis during pregnancy and breastfeeding and safe obstetric practices as recommended by the specific national and international guidelines. Considering that the rate of HIV vertical transmission in Cameroon remain high, the aim of this study is to compare the factors influencing the outcome of prevention of MTCT practices in the context of three different regions of the country.

Methods. This observational-descriptive study compares the growth (weight, height) rate and morbidity of children (aged up to 6 months) born from HIV positive and negative mothers in three regions (West, North and South) of Cameroon. Data collected are analyzed using the Epi-Info 7 and SPSS 22 software, with a significance threshold of 0.05.

Preliminary results. After obtaining ethical clearance and mother informed consent, the mother-child pairs are enrolled. Enrollment of mother-child pairs is ongoing. Currently, a total of 22 HIV-exposed and 44 HIV-unexposed children are included in the follow-up. The majority of HIV-positive mothers (86%) is taking an ARV-therapy (combination of Tenofovir, Lamivudine, Efavirenz) since > 1 year. The mean of birth weight was 2,860 g and 3,350 g for HIV-exposed and unexposed children respectively. In term of morbidity, during the first two months of both groups children follow-up, those born from HIV exposed mothers had an average of one (01), two (02) and one (01) episodes of malaria, cough and influenza respectively; depending on the climate season.

Conclusions and perspectives. We note a slight difference in the growth of children born to mothers exposed and not exposed to HIV. An analysis of socio-anthropological and maternal adherence factors could explain this difference.

CHARACTERIZATION OF INVASIVE *NEISSERIA MENINGITIDIS* SEROGROUP C ISOLATED IN ITALY

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Background. Meningococci of serogroup C (MenC) belonging to clonal complex (cc) 11 are widely considered able to cause epidemic and outbreaks. Identify and characterize the molecular features of this strain is a priority for public health purpose. In Italy, the introduction of the meningococcal C conjugated vaccine (MCC) in 2005 has led to a reduction in the cases of serogroup C disease mostly among children for whom the vaccination is targeted. However, Invasive Meningococcal Diseases (IMD) due to MenC:cc11 strain are still spreading through the country with high morbidity and mortality. The project aims to molecular characterized the invasive *N. meningitidis* serogroup C collected in the country using a Whole Genome Sequencing (WGS) approach and to compare the genomes from sporadic cases with those from outbreak cases in order to identify specific genes signatures peculiar of hypervirulent MenC:cc1. Finally, we evaluate phylogenetic relationships and the strain origin of MenC.

Methods. Bacterial isolates and clinical samples (blood or cerebrospinal fluid) from IMD cases are collected and characterized at the National Reference Laboratory of Istituto Superiore di Sanità in Rome. Phenotypic and genotypic characteristics, including serogroup identification, multilocus sequence typing (MLST) and antigen type were performed following standard procedures. The complete genome sequences of meningococcal isolates will be obtained using Illumina MiSeq and analysed using the PubMLST database (https://pubmlst.org/neisseria/).

Results. Currently, a total of 48 meningococci of serogroup C from IMD cases were identified and characterized. Three different clonal complexes (cc11, cc334, cc10217) and 6 genotypes, (C:P1.5-1,10-8:F3-6:ST-11(cc11), C:P1.5,2:F3-3:ST-11(cc11), C:P1.5-1,10-8:F1-5:ST-11(cc11), C:P1.7-4,14-6:F3-9:ST-1031(cc334), C:P1.7-4,14-6,F3-9:ST-10134(cc334); C:P1.21-15, 16-50:F1-7:ST-10217(cc10217), were detected. Whole genome sequencing was performed on 26 MenC isolates and compared using a "gene-by-gene" approach available through the PubMLST Genome Comparator. Genomes are clustered by clonal complex; in particular, MenC:cc334 grouped together, whereas MenC:cc11 splitted in subgroups: C:P1.5-1,10-8:F3-6:ST-11(cc11) and C:P1.5,2:F3-3:ST-11(cc11).

Conclusions. Final data of this study will permit to define the main traits of MenC invasive strains currently circulating in Italy.

TOXICOLOGICAL AND LEGAL ASPECTS ON ROAD SAFETY

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Background. This project aims to plan and to implement ad hoc protocols for management of forensic toxicological analysis in compliance with the Italian laws on road safety (artt. 119, 186, 186-bis, 187 c.d.s., art. 589-bis and 590-bis c.p.), engaging Law Enforcement Agencies, National and Regional Institutions, Health-care personnel and forensic toxicology laboratories.

Methods. These protocols will be conformed the forensic toxicological and legal-medical requirements and will punctually describe the analysis purposes and the operational modes. In particular, the operational modes deal with all the necessary procedures including the request modality by Law Enforcement Agencies and the informed consent. Special attention is focused on the collection and management of biological samples, the chain of custody and the analytical toxicological analysis. Development and validation of specific analytical methods are a second goal of this project. In particular, methods for detection and quantification of alcohol and its direct markers, such as ethyl-glucuronide and fatty acids ethyl esters and illicit drugs (and their metabolites) in various biological matrices (i.e. blood, urine, oral fluid, scalp and body hair). Besides classical drugs of abuse, the so called New Psychoactive Substances (NPS) will be also monitored with the application of the most modern analytical techniques.

Results. In order to plan new protocols, I started studying the ones adopted by the Department of Health Science of University of Florence. Here I studied three principal aspects:

- Traffic law and its application;
- Collection and management of biological samples;
- Forensic toxicological analyses.

Conclusions. During my first year of PhD, I was able to study an effective protocol, in order to obtain a full comprehension of critical aspects, such as sample collection, forensic toxicological analysis, drug panel.

THE EVALUATION OF PALLIATIVE CARE AND THE NEEDS IN PRIMARY HEALTH CARE IN VLORA CITY COMMUNITY

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Background. The management of palliative patients is a challenge of health care workers. In order to be closer to the needs of these patients, the approach used in palliative care of hospice service and residential care has helped the families and their families to find solutions for these issues up to the terminal death phase. Studying the needs of cancer patients is fundamental in order to build models where the service offered is appropriate to the patient needs and is accessible from everybody. The management of these patients requires a multidisciplinary approach closer to the patient and their needs, based on the law for palliative care in primary health care.

Methods. This is a quantitative, cross sectional study, based on the data obtained from the questionnaires filled from health care workers of primary care in the city of Vlore, patients and community. The inclusion criteria: the patients diagnosed with tumors, their family members, and health care personnel. After a careful literature review, we selected the proper instruments in order to evaluate the experiences of the patients in primary care, the awareness of the community for palliative care and the assessment of the health care providers with the instruments:

- Patient/client experiences, patient questionnaire, Modified from: The Patient Outcome Scale;
- Community Awareness of Palliative Care- CHSD;
- Palliative Care providers- Modified from: Promoting Excellence in End-of-Life Care.

Results and conclusions. The data obtained will describe in detail the actual situation in order to better organize the palliative care in primary care, the needs of the patients and the community. These results will be used to develop training programs for the primary health care providers, to develop instruments and models of assistance in palliative treatment, in order to better manage the problems of patients with tumors, in their advanced stages of the disease. The data shows that the palliative care in primary patient care is still dysfunctional and the staff needs training in this field. It is necessary the development of a training program for the nurses and enhancing their practice skills in palliative care.

New research topics

INTEGRATING HEALTH PROTECTION AND HEALTH PROMOTION TO FOSTER EMPLOYEE WORK ABILITY AND ACTIVE AGEING

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Background. The obesity of the workforce is one of the greatest public health challenges of the 21st century. Based on the latest estimates in European countries, overweight affects 30-70% and obesity affects 10-30% of adults. On the other hand, Europe's workforce is ageing: by 2030, workers aged 55-64 are expected to make up 30% or more of the total workforce in many countries. Combination of these factors implies an increasing number of workers with health problems and decreasing ability to work. Growing evidence indicates that comprehensive policies and programs that simultaneously address health protection and health promotion may help counteract this trend.

Objectives. This study has a twofold aim: on one hand it aims to identify the main determinants of health deterioration and inability in the Italian workforce by exploiting data of the INSuLa project, a survey on health and safety at work involving workers, employers, occupational physicians, worker safety representatives, prevention and safety service in the workplace. On the other hand, it aims to develop and appraise different programs integrating collective prevention actions, individual health surveillance systems - including the assessment of work ability - and actions aimed at promoting health and active ageing in the working setting.

Expected results. This study may supply evidence of the main socio-demographic and occupational factors influencing employees' personal well-being and work-related outcomes (e.g., work ability), as well as those fostering the development of sustainable working conditions. Furthermore, it could provide important guidance for multifaceted, worksite-based initiatives to promote health and active ageing at both individual and organizational levels.

Future perspectives. The integration of worker health protection and promotion efforts is an area of emerging importance. The findings from this study may contribute to the development of a holistic approach integrating health protection and health promotion and facilitate its application in the Italian workplaces. Furthermore, it may help improve the dialogue between researchers and stakeholders on future-oriented decision making regarding sustainable employment and maintenance of work ability also in consideration of the emerging risks and changes in the world of work.

TUBERCULOSIS IN SYRIA: CURRENT SITUATION AND FUTURE PERSPECTIVES

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Background: Tuberculosis (TB) is caused by bacteria called *Mycobacterium tuberculosis* and it is currently one of the first leading killer infections worldwide. The World Health Organization estimated that 10.4 million people developed TB and about 1.7 million died from the disease in 2016. Crisis, including wars and population displacements, are often associated with up to 20-fold increases in the risk of tuberculosis. In the 21st century, Syrian war can be consider as one of the biggest humanitarian disasters that caused the largest forced displacement in the world. The civil war that has begun since March 2011 has forced hundreds of thousands of Syrian families to leave their homes. Furthermore, the number of people that officially registered as refugees was estimated to be about 5.6 million. Even though there are no real indicators on the end of the war in the country, there is a policy to return refugees to the safe zones in Syria as soon as possible. This policy follows the aggravation of the refugee crisis in the neighboring countries, especially Lebanon and Jordan. However, Syria does not have the necessary infrastructures and this situation might lead to a further exacerbation of epidemics, including TB in Syria.

Objectives: The main objective is the assessment of the TB in Syria, including the study of the status before the crisis, the current situation and future perspectives. Additional aim is to evaluate the Syrian plan to contain TB, treatment programs and available resources in terms of staff, money, space, time and partnerships.

ONE HEALTH: IMPLEMENTING INTEGRATED EARLY DETECTION FOR ARBOVIRUSES IN MEDITERREAN AREA, BALKAN, BLACK SEA AND SAHEL REGIONS COUNTRIES

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Background. Implementation of integrated surveillance strategies for arboviruses has been central in the networking project called MediLabSecure that involved about twenty non EU-countries (belonging to the Mediterranean area, the Black sea and Balkan regions) from 2014 and 2018. The MediLabSecure 2 (MLS2), supported by EC DEVCO (IFS/2018/402-247), is its natural continuation, and was launched at the beginning of 2019. Moreover, to combine the two, between Nov and Dec 2018 a Conference and a Workshop regarding One Health were organized in Rome and Teramo respectively, and participants were asked to highlight gaps and needs, and priority pathogens, to be addressed in the following period. Seven pathogens of interest were stressed out: Chikungunya virus, Crimean-Congo Hemorrhagic fever virus, Dengue virus, Yellow fever virus, Rift Valley virus, West Nile fever virus and Zika virus.

Objectives. During MLS2 attention is given to the implementation of early detection for arboviruses. A survey is currently under development, aiming at the collection of possible indicators to be used for early detection. The survey is structured in four sections, namely "climate and environment", "vector", "human" and "animal". In each section, six to ten indicators are presented and recipients will be asked to answer about the modality of indicators' collection and storage. The survey is targeted to the recipients expertise: medical entomology, human virology and public health, and animal virology and animal public health. Data are to be collected per each one of the relevant pathogens at a country level, in the 22 countries involved in the MLS2. The survey will be available for compilation for about two months.

Expected results. Desired output would be information on what are the beneficiary countries of MLS2 doing at present during surveillance activities for relevant pathogens, in terms of: number of indicators collected, specific type of indicators collected, level of data collection, modality of data storage, institution in charge for data collection, etc. Preliminary results of the survey will be presented during the Kick Off Meeting (KOM) of MLS2, expected for July 2019, Paris.

Future perspectives. On the basis of the output of the survey, its preliminary presentation during the KOM and the feedback received from the countries' representatives during the abovementioned meeting, two or three countries will be selected for further in-depth studies during site visits.

ACADEMIC EDUCATION OF MEDICAL AND HEALTH PROFESSIONS STUDENTS FOR HEALTH EQUITY

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Background. In the last years, the Global Health (GH) and Social Determinants of Health (SDH) approach has started to spread in Medical Schools and other Health Professions Courses. In Italy, the debate related with GH Education has begun with the Italian Network for Global Health Education (INGHE) in 2009. Actually, in many Italian Medical Schools there is a GH Elective. It is necessary to share reflections and documents related with GH Education to stimulate a debate in the academic world so that this approach become mandatory in academic curricula.

Objectives. The main objective of this research is to give a substantial contribution to the education of medical and health professions students in the field of SDH and Health Equity, with particular reference to Migrant Health. In the perspective of transformative learning, the aim is to let future health professionals become aware of their social responsibility and commit themselves to act against health inequities.

Expected results. A literature search has been conducted on PubMed, Scopus and Web Of Science, using key words related with "GH", "Undergraduate Education" and "Migration". The literature search is actually ongoing but it is possible to summarize some important points. There is a growing number of academic educational experiences related with GH and SDH, but few specific experiences concerning the aspect of Migration and Health.Interactive teaching methods, better if organized with the direct collaboration of students, are more effective. Experiences in the field, especially in peripherical areas and with marginalized people, are important to influence the intention of students to practice in underserved areas. Professor M. Marmot has been interviewed regarding the education of medical students on SDH approach and Health Equity.

Future perspectives. At Sapienza University a GH Elective course is offered to students of various Courses and Faculties since 2008. In the last years also different 'GH Gyms' (as the authors call GH Experiences) have been proposed to medical and health professions students, in the field of "Migration and Health" and of "Prison and Health". An online survey has been prepared to evaluate, after some years, the impact of these educational experiences on the decisions of future health professionals to commit themselves to act against health inequities. The thesis of the authors is that these educational proposals are of vital importance for the graduate's future ethical role in the society and should be considered directly related with University's Third Mission.

INTEGRATIVE METAGENOMIC AND CULTUROMIC APPROACH TO STUDY TEMPORAL DYNAMICS OF SKIN MICROBIOTA IN ATOPIC DERMATITIS

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Background. Skin Microbiota (SM) ensures the maintenance of skin health by promoting normal immune system functions, by controlling inflammatory processes and preventing pathogens' colonization. The same skin microenvironments are characterized by a common core of microbial communities; sebaceous sites are dominated by lipophilic *Propionibacterium* species and moist areas are colonized by *Staphylococcus* and *Corynebacterium* species. It has been hypothesized that alterations of SM may be associated with progression of Atopic Dermatitis (AD), a chronic inflammatory skin disease, clinically characterized by dry, red, itchy skin lesions. The pathogenesis of AD is not well understood, but interactions between defective skin barrier, recurrent infections and immune system imbalance have been associated to the AD development. Metagenomic studies of SM in the inflamed atopic skin revealed changes in bacterial composition during flare, with decrease in the genera *Streptococcus, Corynebacterium, Propionibacterium* and in *Proteobacteria* and increase of members of the genus *Staphylococcus,* in particular *S. aureus*. However, to date the functional consequences of the dysbiosis that occur during the course of disease are poorly understood.

Objectives. The aim of my research is to analyze the microbial temporal dynamics of SM in AD patients during the disease course. In particular, the quali-quantitative variations of different microbial taxa at different phases of the disease (baseline, flare, post flare) and the functional differences between strains isolated from single species will be evaluated.

Expected results. Integrative metagenomic and culturomic approaches will allow to capture the full genetic potential of SM in AD patients: to determine the composition of SM concerning strains within a single species, to evaluate the functional consequence of strain-level differences between patients and in the different stages of disease and to study interactions between different bacterial strains present in the SM.

Future perspectives. Species and strains obtained by culturomics will allow to develop *in vitro* and *in vivo* models to analyse the interactions between mutualistic bacteria, pathogens and host in order to elucidate their role in the disease and healthy as an important step in the development of prebiotic and probiotic strategies and new drugs.

CORRELATION BETWEEN EGO-SYNTONIC INFORMATION SELECTION AND PERSONALITY PATTERNS

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Background. In the health care field, disinformation is a widespread practice, especially regarding the topic of vaccination coverage. In recent years, studies that has focused on the observation of users behaviour, especially during fruition pro and anti-vaccine pages inside social networks, has shown how the effect of "selective exposure" to non-truthful content within social networks produces a large influx of users who draw information from the "no-vax" pages without any control about the sources. Polarization of users on social networks provides a useful clue to understand the phenomenon called "misinformation" whereby a subject becomes an "involuntary" agent of the spreading of mistaken information outside the virtual context.

Objectives. The purpose of the present study is to investigate whether exist a relationship between personality patterns and the ways used by the subjects to select informations recognized as "ego-syntonic." The following areas will be explored:

- beliefs related to pharmaceutic, vaccines and complementary and alternative medicine (C.A.M.) treatments;
- personality patterns assessed through the administration of personality questionnaires (Minnesota Multiphasic personality inventory-2, Personality assessment Inventory, Big Five questionnaire and 16-PF);
- administration of self-report questionnaires that assess the presence of sceptical attitudes or non-objective thought that concern health-care topic (conspiracy beliefs scale, vaccine conspiracy beliefs scale, Vaccination Attitudes Examination Scale);

Expected Results. Our expectations are to see that subjects who totalize higher scores on the scales focused on the assessment of specific personality patterns (for example the Pa scale of MMPI-2) are more inclined to mark the items focused on conspiracy beliefs and mistaken beliefs towards pharmacological and medical treatments.

Future Perspectives. Our study could suggest how the detection of a set of specific personality models can be correlated with the mode of selection of information that is recognized by the subject as ego-syntonic, as suggested by the "confirmation bias" theory. Our expected findings could be useful to improve the "health communication techniques."

REVIEW ABOUT APPLICATION OF LAW 24/2017 (GELLI) DURING THE FIRST FIVE YEARS SINCE ITS ENTRY IN FORCE

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Background. In the last decade we have witnessed a profound change in medical liability, passing from an extracontractual conception to a contractual one, aimed at protecting the patient's interests. The new law 24/2017, on the contrary, is aimed at ensuring a more favourable position for healthcare professionals without compromising the protection of the patient's right to health. Furthermore, the law clarifies that public or private providers of health care are in charge of refunding patient involved in a *medical malpractice* lawsuit. Nevertheless, providers of health care are entitled to recoup the refund from healthcare professional. More specifically, article 5 clearly identifies the need for healthcare professionals to constantly refer, in the provision of every assistance service, to the recommendations provided for by guidelines issued by accredited scientific societies. A further innovation, expressed by Article 8, is the introduction of a preferential procedural way, represented by the performance of a preventive technical consultancy as provided by article 696bis of the Code of Civil Procedure. In article 13, on the other hand, it is specified how healthcare providers are supposed to communicate their involvement in the judicial field to the healthcare professional operator. Finally, Article 15 states the importance of the establishment of an expert panel composed of a medical examiner and one or more specialists, chosen on the basis of the subject matter of the case in question, both in criminal and civil proceedings.

Objectives. The purpose of this study is to evaluate how the law 24/2017 has been concretely applied in the first five years following its entry in force. In particular, not being able to assess all the legislative innovations required by this law in such a short period of time, we aim to focus our attention on the elements provided for in articles 5-8-13-15. As so, the following will be evaluated: adherence to the guidelines as a means of evaluating the work of health professionals; the use of preventive technical advice (as required by article 696bis); the involvement of the healthcare professional in the civil procedure; the establishment of specialist board in the assessment of professional responsibility litigations.

MULTIPLE IMPLICATIONS OF POST-MORTEM COMPUTED TOMOGRAPHY (PMCT) IN THE FORENSIC APPROACH TO CHARRED BODIES

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Background. PMCT provides important supplementary information to the traditional autopsy and areas not routinely investigated during the autopsy (facial skeleton, basilar skull, cervical spine, limbs). PMCT provides others advantages, such objectivity, repeatability, 3D rendering. In the case of burn victims, the advanced state of carbonization complicates the dissection and some foreign bodies (bullets, prostheses, etc.) or bone alterations (osteosynthesis, traumatic fractures, etc.) could be missed.

Objectives. The aim of this project is to realize an operative protocol that provides to the radiologist the keys to establish a complete and focused reports in all cases of PMCT of burn victims. The radiological investigation will be addressed according to the specific needs of the case, in order to differentiate between normal post-mortem changes from heat-related changes and to help the pathologist in different issues, ranging from gender identification, to localization of foreign bodies, or sites for fluid/DNA sampling.

Expected results. PMCT will allow to differentiate between normal post-mortem changes from heat-related changes, helping the pathologist in victim's identification and in localization of possible sites for collecting DNA/fluid samples.

Future perspectives. The idea is to use the results obtained to optimize, validate and promote the operative protocol used in such a way it can be consistently applied in all cases of burned/charred bodies. According to the needs, the radiologist must discern all the contextual divergences with the forensic history, and must be able to report all the relevant elements, in order to answer to the following questions:

- Are there features that could help in victim's identification? [Presence of metallic objects stuck inside the body or medical devices useful to be reported in order to correlate with the medical record of the alleged victim. In extreme cases, where victim's secondary sexual characteristics are no more distinguishable, uterus or prostate are most often present on PMCT, allowing to determine the subject's gender]
- Is there evidence of biological fluids available for toxicological analysis/DNA sampling? [In addition to toxicological screening, the percentage of carboxyhaemoglobin must be ascertained to determine whether death occurred before or during the fire. PMCT can show possible collecting sites and avoid loosing fluids during dissection]
- Is there another obvious cause of death than heat-related lesions? [PMCT will show the presence of foreign bodies (bullets, knives, blades, etc.) or radiological

findings different from typical heat-related lesions (bone fractures different from typical heat-related fractures, epidural collections with a subdural appearance, ecc.) that are able of causing traumatic death].

EPIDEMIOLOGY AND CLINICAL IMPACT OF AIRWAYS COLONISATION FROM NON-*ASPERGILLUS* FILAMENTOUS FUNGI IN ADULT PATIENTS WITH CYSTIC FIBROSIS: A PROSPECTIVE STUDY

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Background. Cystic Fibrosis (CF) is the most common lethal genetic disorder among Caucasians, with an average estimated prevalence of 1:3000 in Europe, North America and Australia. CF is typically characterized by chronic airways infection from a wide spectrum of pathogens, classically including Pseudomonas aeruginosa and Staphylococcus aureus. Chronic fungal infections are commonly encountered in this population as well. These are frequently secondary to *Aspergillus spp*.; however, isolation of clinically significant Non-*Aspergillus* Filamentous Fungi (NAFF) from patients with CF has been increasing over the past decade. Nevertheless, their real prevalence, and consequently, their clinical impact on CF outcomes is hard to estimate due to different sputum processing protocols across laboratories. Thus, routine respiratory sampling and processing may significantly underestimate the true prevalence of NAFF in CF, preventing to precisely assess their role in the natural history of the disease.

Objectives. Primary aim of the present project is to compare the prevalence of respiratory tract colonisation from NAFF in a large cohort of adult CF patients obtained by the adoption of Extended fungal Cultures (EC) compared to routine laboratory cultures. Secondly, we aim to assess the effects of colonisation from NAFF on the most important clinical outcomes in CF, as lung function decline rate, Pulmonary Exacerbations (PEx), hospital admissions, nutritional status and survival.

Methods. In a 2-year observational period, sputum samples will be collected from adult CF patients attending their routine clinical assessment at the outpatient clinic of the Adult CF Centre of Policlinico Umberto I Hospital' (approximately one visit every three months). Two samples will be collected for every patient at every visit: one will be processed with routine laboratory protocol, the other one will be processed with EC. These consist in: sample's mucolysis, dilution and homogenization, use of selective growth media (i.e. Sabouraud dextrose agar) enriched with anti-*Pseudomonas* antimicrobial agents and incubation at 30-35°C for 6 weeks, in order to allow the eventual isolation of slow-growing fungal species, such as Exophiala spp. Clinical outcomes will be monitored and registered for each participant at every visit, as routinely done during patients' regular follow-up.

Expected results. We expect to find: 1) a significantly higher detection rate in NAFF airways colonisation from EC compared to routine processing protocols; 2) a prevalence of NAFF ≥20% among CF adult patients; 3) a significant negative impact from NAFF

colonisation on lung function decline rate, PEx, hospitalizations and nutritional status. We will demonstrate that the use of properly designed culture procedures is essential to correctly assess the prevalence and the clinical impact of NAFF in CF.

HEPATITIS E VIRUS INFECTION AND DEMYELINATING DISEASES: EPIDEMIOLOGICAL STUDY OF HEV SEROPREVALENCE IN PATIENTS AFFECTED BY CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY (CIDP) AND AMYOTROPHIC LATERAL SCLEROSIS

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Background. Hepatitis E Virus (HEV) is a major cause of viral hepatitis in humans worldwide. Seroprevalence studies carried out in various European countries have reported high rates of anti-HEV IgG antibodies among the general population In Italy, a recent large-scale, nationwide study indicated that during 2015-2016 the prevalence of anti-HEV IgG and IgM among adult blood donors was 8.7 and 0.4% respectively. Several extrahepatic manifestations have been reported in association with acute and chronic hepatitis E virus infection. The most common are neurological, occurring in 8% of infections: Guillain-Barré syndrome, neuralgic amyotrophy and encephalitis. In particular, anti-HEV IgM antibodies were demonstrated in 5.0% of patients affected by AIDP, compared with 0.5% of the healthy controls (OR 10.5, 95% CI 1.3-82.6, p=0.026). Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is an acquired immunological-based neurological disorder closely related to Guillain-Barré syndrome and it is considered the chronic counterpart of that acute disease. Although the cause of CIDP remains unclear, it has been associated with multiple triggers, including viral infections. Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disorder, characterized by a rapidly progressive degeneration of upper and lower motor neurons, which results in muscle weakness and wasting. The pathogenesis of ALS remains largely unknown. It has been hypothesized that the occurrence of the disease could be due to genetic predisposition, triggered by the exposure to environmental risk factors. At present, there is not evidence in literature of HEV seroprevalence in patients affected by CIDP and ALS, although the virus may have a direct or indirect role in their pathogenesis.

Objectives: Aim of the study is to evaluate the prevalence of HEV infection in patients affected by CIDP and ALS, compared to healthy controls (caregivers).

Methods. Plasma samples will be tested for IgG and IgM anti-HEV and for HEV RNA using validated assays.

Expected results. From the analysis of the obtained data, we expect a higher HEV seroprevalence in patients affected by CIDP and/or ALS compared to healthy controls.

Future perspectives. Although HEV is becoming increasingly recognized, the causal link with neurological manifestations remains to be established. The possible association of CIDP and/or ALS with a higher HEV seroprevalence, compared to a control healthy group sharing the same dietary habits, could suggest a correlation between hepatitis E and the neurological damage associated with these demyelinating diseases.

THE OBSTRUCTIVE SLEEP APNEA SYNDROME (OSA) AT WORK

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Background. OSA is a chronic disease with significant economic and social impacts, with a high prevalence in general population, particularly concerning to road and work-related accidents. The undiagnosed and undertreated cases are about 40-70%. In 2001, among the male adult European population (30-70 years) a prevalence of the mild OSA - Apnea Hypopnea Index (AHI) ≥5 - of 26% has been reported, while the moderate-severe OSA (AHI≥15) represented the 14%. In 2013 Peppard (2013) showed that out of 1520 participants (age 30-70 years): 33.9% of men (43.2% over 50 years) had at least one AHI≥5, half of them had daytime sleepiness and 13.0% reported an AHI≥15. More recently, a study conducted by Heinzer (2015) on a large group of Swiss population sample (2121 subjects; age 40-85 years) has reported a prevalence of moderate-severe OSA (AHI≥15) in 49.7% men and 23.4% women subjects. In Italy the prevalence data are not reported: recent studies estimate about 6 million people with OSA (2 million with a full-blown picture) while the undiagnosed cases would be estimate around 40-60%.

Objective. The project aims to improve a better knowledge of OSA investigating the relationship between OSA and oxidative stress and OSA and comorbidity, through the study of specific early markers. The identified markers could be proposed in clinical practice to integrate the diagnostic methods currently in use in occupational health surveillance.

Expected results. The study will contribute to improve the early detection, identification and knowledge of the OSA; the aim is to propose an OSA's evaluation/surveillance clinical protocol; it will contribute to develop the "best practices" for the prevention of accidents at work related to OSA.

Future perspectives. The results could improve the health occupational strategies for the early identification of the OSA in general population and workers. A program of primary and secondary prevention for OSA with the positive effects on health and social costs, will contribute to reduction of the OSA's comorbidities and the number of road accidents also related to work.

POST-ARRIVAL SCREENING FOR MALARIA IN ASYMPTOMATIC SUB-SAHARAN ASYLUM SEEKERS IN ITALY

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Background. Over the last decade, Europe has experienced an increasing influx of migrants undertaking the perilous Mediterranean Sea crossing, looking for protection and/or improved living conditions. Malaria is a significant health risk for refugee populations originating from endemic areas, but there is presently no consensus on the best way to screen the mobile population for malaria. The possible presence of gametocyte-carrying subjects could represent an important risk factor for the re-emergence of the parasitosis in Italy where the potential vectors of the parasite are still present.

Objectives. The purpose of the present study was to evaluate the different diagnostic methods for detecting the Plasmodium spp. in semi-immune asymptomatic migrants.

Methods: A single venous EDTA-blood sample was collected by venipuncture from 55 consecutive newly arrived asylum seekers hosted at the Asylum Seekers Centre of Castelnuovo di Porto, who fulfilled the criteria: arrived in Italy crossing the Mediterranean Sea within the previous 7 days and native of one of the sub-Saharan African countries. Samples were analysed for Plasmodium parasites by Light Microscopy (LM), Rapid Diagnostic Test (RDT), PCR and Loop-mediated isothermal amplification (LAMP). Diagnostic accuracy endpoints (sensitivity, specificity, predictive values, and kappa coefficient) of RDT, PCR and LAMP were compared with LM as the gold standard method and between LAMP and PCR.

Preliminary results. Of the samples screened, only one subject was positive in LM with very low parasitemia. The same subject resulted positive for RDT and LAMP but not for PCR. Of the 54 smear-negative subjects tested six resulted positive for Plasmodium DNA with LAMP, none with standard PCR and one was found RDT positive. The microscopy gave a higher level of agreement with PCR and RDT (both of them 0.98) and near-perfect specificities (98%) and sensitivities (100%) with RDT. LAMP reported a sensitivity value of 100% because it allowed the identification of 6 positive cases that were negative on morphological examination. The specificity value was slightly lower when compared to PCR (88%). Overall agreement between LAMP and PCR was 0.87 (kappa value).

Future perspectives. Microscopy remains the gold standard for the diagnosis of malaria as it has shown the greatest performances in comparison with the other diagnostic methods. LAMP- simple, rapid and accurate molecular tool represents a highly sensitive and less complex alternative to PCR-based tests particularly in cases with sub-microscopic infections outside reference laboratories. Although the clinical relevance of low-parasitaemia asymptomatic cases needs to be further investigated, the current findings highlight the need to revise the current surveillance system in migrants, relying on LM and RDTs only.

A MEDICO-LEGAL POINT OF VIEW ON PRETERM NEWBORNS MALPRACTICE CLAIMS

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Background. Preterm birth is an emerging health problem if we consider that each year, only in Italy there are about 33,000 preterm newborn. Therefore, prematurity is globally an important cause of mortality and morbidity, as well as be responsible for the significant direct and indirect economic burdens. In fact, each preterm can increase extra in-hospital costs of about 93,000 dollars. In addition, medical malpractice claims on premature infants can be extremely expensive for physicians and health care facilities considering that preterm is involved in about 12% of all medical malpractice claims for cerebral palsy.

Objectives. This study wants to give a retrospective descriptive analysis of medical malpractice claims database of one of the largest Children Hospital in Italy, to identify which are involving preterm newborn. The aim is to evaluate how many medical malpractice claims are strictly related to prematurity and most important complications (infection, neurodevelopmental deficit, neurological, visual impairment).

Preliminary results. In a global of 485 claims, only 26 were related to a preterm and 3 of this are related to extremely low weight births. Our data showed that most cases of malpractice claims related to prematurity are ineligible for refreshment, as the claimed damages should be a direct consequence of prematurity itself. Prematurity is, in fact, a condition that exposes to a high risk of developing complications, many of which although they are predictable remain inevitable.

Future perspectives. Among the possible strategies, better communication could be an effective and simple solution that can implement compliance between patients and physicians. Better communication in order to prematurity complications can be a valid instrument to prevent many of malpractice claims. At the same time, improvement of health technologies will allow, as already documented in recent years, a better long-term outcome of preterm.

WHAT IS THE RELATIONSHIP BETWEEN PHYSICAL ACTIVITY AND HEALTH? EVIDENCE FROM EXPERIMENTAL AND OBSERVATIONAL STUDIES

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Background. Physical Activity (PA) and exercise have beneficial effects on health, and everyone can profit from becoming more physically active**.** According to the World Health Organization, physical inactivity is the fourth leading risk factor for global mortality accounting for approximately 3.2 million deaths annually and reducing the risks for more than 25 chronic medical conditions. Most studies have highlighted the advantageous of (PA) to decrease pain and promote flexibility and function of different parts of body and muscle function. Exercise Training (ET) leading to improved levels of cardiorespiratory fitness, kind of cancer, diabetes, ischemic stroke, cardiovascular dieses and est. International physical activity guidelines generally recommend 150 minutes per week of moderate- to vigorous intensity physical activity.

Objectives. Health-related physical fitness is consistently associated with greater risk reductions. PA is a well- established primary and secondary preventative strategy against at least 25 chronic medical. The principal aim of thesis will be demonstrating the relationship between physical activities and health in different settings and populations.

Expected results. Physical activity reduces the risk for mortality and chronic diseases**,** and as a health promotion improve life style, and psychological factor and functional cognitive in adult and older people. The relationship between PA and health will be looked at using different study design (experimental studies, as well as cohort, case-control and cross-sectional studies) and setting (general population, Healthcare professionals, women with breast cancer).

Future perspectives. In the world of personalized medicine, it is important to consider physical activity as one of the main tools for maintaining and improving peoples' health, both at the individual and collective level.

STUDY OF PERSISTENT ORGANIC POLLUTANTS (POP_S) TOXICITY BY SETTING UP AN *EX NOVO* METHOD BASED ON CHEMICAL IONIZATION MASS SPECTROMETRY

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Background. Micro-pollutants are high toxicity substances with very small concentrations, which include Polychloro-p-dibenzodioxins (PCDD) and Polychlorodibenzofurans (PCDF), Polychlorobiphenyls (PCBs) and Polycyclic Aromatic Hydrocarbons (IPA). The numerous toxic effects of these organic micro-pollutants are linked to their structure-activity relationship. The IARC defined 10 characteristics, called Key Characteristics (KC), that all human carcinogen has in common. These key features have recently been introduced to standardize the research approach, organization and evaluation of mechanistic tests to support the identification of cancer risk. The first KCs links the potential carcinogenicity of a specie to its electrophilic power that could be characteristic or to be induced by metabolic activation that leads to form adducts with DNA.

Objectives. The aim of this project is to study the electrophilic power of organic micro-pollutants by gas phase reactions of different electron-donor species. The assessment of the correlation between toxicity factors of each organic micro-pollutants and their predisposition to ionize in Chemical Ionization (CI) will be carry out by different instrumental settings (GC/MS source) depending on reagent gas.

Preliminary results. Previous studies have shown the connection between POPs factor response in GC/CI-MS with the substituents and stereochemistry of the species. Indeed, they vary according to the inductive effect of the substituents and the resonance effects enhanced by planar compounds. Furthermore, it was observed a greater discrimination using Negative Chemical Ionization (NICI) compared to Positive Chemical Ionization (PICI).

Future perspectives. The goal of this work will be to give a more restrictive definition of the first IARC Key Characteristics (KC). This could help the mechanistic study in the formation of Electrophilic-DNA adducts. If a correlation between POPs factor response in GC/CI-MS and Electrophilic-DNA adducts formation will be proven, it could be extended to known and unknown chemical species in industrial emissions and in ambient air. This allows to consider substances which toxicity has been underestimated until now despite their non-negligible concentrations. It will help to define the presence of potentially toxic volatile and semi-volatile xenobiotics in environmental compartments.

STUDY OF THE GUT-BRAIN AXIS IN HIV+ PATIENTS: EFFECT OF MODULATION OF INTESTINAL FLORA ON PERIPHEAL AND CENTRAL IMMUNO-ACTIVATION STATUS

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Background. Since the early stages of HIV infection (7-14 days) the virus is responsible for the loss of intestinal mucosal barrier integrity this causes an increase in microbial translocation, systemic inflammation and, finally, chronic immune activation. In fact, new scientific knowledge attributes to HIV the systemic damage that occurs during the course of the disease with involvement of the central nervous system. The passage of HIV through the blood-brain barrier causes inflammation at the neuronal level, while the translocation of microbial products from the intestine to the systemic circulation is responsible for inducing a persistent state of neuroinflammation. Therefore, the alteration of the intestinal microbiota is involved in the regulation of various neurocognitive disorders, such as depression and autism, due to the production of neuroactive substances and metabolites. The modulation of the intestinal microbial flora as a supplement to antiretroviral therapy in HIV patients has shown promising results in the ability to regulate the diversity of intestinal microbial species and in restoring immunity to the intestinal mucosa, resulting in a decrease in microbial translocation and immuno-activation.

Objectives. 1) Contribute to identifying metabolic pathways involved in the systemic immunoactivation process and in the central nervous system; 2) measuring immunoactivation levels both in peripheral blood and in the spinal fluid before and after modulation of the intestinal microbial flora; 3) analyze any changes in the metabolism of some aromatic amino acids (phenylalanine, tyrosine, phenylalanine/tyrosine) that are observed during HIV infection before and after modulation of the intestinal microbial flora; 4) analyze the protein content of the cerebrospinal fluid before and after modulation of the intestinal microbial flora.

Expected results. The aim of the project is to evaluate the link between the modulation of intestinal microbial flora and the peripheral inflammatory state and central nervous system.
The patients involved in the project will be enrolled at the Department of Public Health and Infectious Diseases of the Policlinico Umberto I (Sapienza, University of Rome). They will be collected, first (T0) and after six months (T6) the administration of a probiotic multistrain formulation, blood, faecal, cerebrospinal fluid samples. The study currently includes 6 HIV positive subjects on stable and effective antiretroviral therapy and 6 healthy controls. In both populations we collected: a fecal sample that will be analyzed by NMR for the evaluation of the metabolome, a blood sample to search immuno-activation markers such as CD-38 and HLA-DR by cytofluorimeter. Further analyzes will be performed to assess the levels of inflammation and immuno-activation in the gut and central nervous system. Finally, the number of enrolled patients will be increased in order to achieve statistical significance.

ZEBRAFISH: A POWERFUL TOOL IN HEALTH AND ENVIRONMENTAL STUDIES

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Background. There is an increasing scientific evidence that the discharges, releases and emissions of multiple chemical contaminants in the ecosystems (more than 100,000 are the substances registered by REACH) from point and diffuse sources are causing a deterioration of ecosystems and a progressive loss of biodiversity. Every sign of alteration of the system should be considered a possible warning indicator for the human and the environment health. Chemical analysis/monitoring alone is not able to detect the presence of large quantity of substances such as emerging contaminants or mixtures, for this reason an ecotoxicological approach is highly recommended by the scientific community to protect the ecosystem. In this context Zebrafish is considered a valid and promising tool because of its numerous advantages in the ecotoxicological studies, different endpoints indeed can be measured simultaneously giving a more detailed description of different modes of action of the substances.

Objectives. In this project, zebrafish embryos will be utilized to better understand and to describe the effects of the main emerging contaminants (e.g. PFAS, pharmaceuticals) through the application of the "Fish Embryo toxicity Acute (FET) test" (OECD 236, 2013). Four apical observations are recorded as ecotoxicological endpoints of lethality: coagulation of fertilised eggs, lack of somite formation, lack of detachment of the tail-bud from the yolk sac, and lack of heartbeat. In order to identify the main action mechanisms of contaminants, sublethal effects such as deformities, heart beat rate, spontaneous movements, flow blood and behaviour will be detected with specific software. Information on genotoxic effects will be also acquired applying the genotoxicity test "Comet assay" to the embryos of zebrafish. Single substances and simple mixtures of them in laboratory will be analyzed and it will be conducted an environmental sampling in the urban section of the Tiber River in the city of Rome. The results will be evaluated together with other informations deriving from institutional chemical monitoring programmes and other studies conducted in the area.

Results and future perspectives. The results of the project will contribute to: 1) increase the efficiency of the zebrafish test in order to detect several dangerous chemicals that are present in the ecosystems and potentially harmful for human health; 2) improve the knowledge of the chemical mode of actions of the main emerging contaminants; 3) support the national and European legislation for the implementation of monitoring plans of aquatic ecosystems.

OCCURRENCE, DISTRIBUTION AND ECOLOGY OF ANOPHELES MOSQUITOES AND RISK OF MALARIA RE-EMERGENCE IN ITALY

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Background. Malaria is a disease caused by several species of protozoa of the genus *Plasmodium*. An increasing number of imported malaria cases by travelers and immigrants from endemic regions have been reported in several European countries. The recent autochthonous cases of malaria occurred in 2017 in Italy have renewed the interest for a disease eradicated many years ago. The prevalence and incidence of malaria are closely related to the presence of the vector in a geographic area. Malaria is vectored by a number of mosquito species of the genus Anopheles, which plays both the role of carriers and of definitive/alternative hosts. Other key parameters for the spread of malaria are the density of mosquitoes, their longevity and tendency to bite humans, the climatic conditions and the number of infected people. Several Anopheles species competent for malaria transmission occur all over Europe. The most common belong to the *Anopheles maculipennis* complex, including species indistinguishable morphologically with a variable susceptibility to the infection by different Plasmodium.

Objectives. Although the risk of malaria re-emergence in Europe and Italy is currently considered low, changes in habitat structure and adaptation to the urban environment of anophelines provide new opportunities for malaria transmission and emergence. The principal aim of this study is to evaluate the current risk of re-introduction and emergence of autochthonous cases of malaria in northern Italy assessing the current presence, density, and distribution of Anopheles mosquitoes and their role in the malaria circulation.

Expected results. A check list of Anopheles species present in northern Italy will be obtained. Monitoring of the mosquito larvae will give information on which environments are suitable to the development of the different Anopheles species; driving the control actions with a low environmental impact. Adult mosquitoes will be monitored and identified using different methods, some of them not tested yet.

Future perspectives. We expect to have a model built with local data able to estimate the risk of re-emergence of malaria in northern Italy, considering different future scenarios. The project will obtain an evaluation of the areas at risk of malaria emergence following an undetected or late detected human case. This will guide the preventive measures to be taken in particular risk areas and the emergency actions of disinfestation in case an outbreak occurs.

MONITORING SYSTEMIC AND MUCOSAL IMMUNITY IN HIV POSITIVE WOMEN RECEIVING ANTIRETROVIRAL THERAPY: EVALUATION OF BIOMARKERS AND ENVIRONMENTAL STIMULI

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Background. HIV infection occurs in both men and women, but women face a greater risk to acquire the infection due to substantial mucosal exposure to seminal fluids, HPV infection, menstruation and other gender specific manifestations such as fungal infections of the vagina. This also affects their sexual health and behaviour. Apart from this, invasion by the antigen also has enormous clinical effects which are responsible for the activation of cytokines and biomarkers such as CXCL10, sCD163, sCD14 which are a cascade of proteins activated as a result of heightened innate and specific immune response. Advancement in antiretroviral therapy has been an efficient source for controlling the spread of infection by reducing the viral load, but an immune inflammation persists to different extents depending on clinical situations.

Aim. Evaluate the systemic and mucosal immuno-inflammatory status of HIV positive women receiving antiretroviral treatment.

Methods. Inclusion criteria for subjects: age more than 18 years, absence of acute infection and vaginal discharge, no menstruation, 2 days abstinence, on stable ART with HIV-RNA <20. Lymphocytes (CD4 and CD8), NK and B cells were detected by cytometry, sexual hormone by CLIA assay and IL-1beta, IL-6, IL-8, sCD14, sCD163 were measured by ELISA kit (R&D) on plasma samples and vaginal lavage. Cervical swabs were used for genotyping. Statistical analysis was performed using PRISM 8.0.

First results. Plasma levels of the sCD163, IL 6, CXCL-10 were significantly higher in HIV positive women as compared to healthy donors ($P<0.001$), while IL-6 and IL-8 seemed to be lower in the vaginal lavage of HIV subjects. Moreover CXCL-10 is correlated to plasma estradiol levels ($r=0.8$, $P=0.02$). No shedding of CMV was found at circulatory and mucosal levels, whereas CMV-Ab levels were higher in HIV+ women correlating with IL-1 beta.

Future perspectives. We tend to enrol a greater number of women (infected and uninfected) with different ages to better understand the role of this persistent immune inflammation despite successful antiretroviral therapy. Moreover, at the mucosa level balance within pro anti-inflammatory cytokines, factors like the micro-biome will be studied.

STUDYING OF EXTRACELLULAR PROTEINS OF *ASPERGILLUS*

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Background. Bronchopulmonary aspergillosis is a pulmonary disease that often occurs in patients with asthma or cystic fibrosis. In most published studies, the prevalence of pulmonary aspergillosis is about 8.9% in patients with cystic fibrosis. In particular, the prevalence of pulmonary aspergillosis is about 1.9-10.8% in USA; 8.75% in *Great Britain*; 5-8% in Europe. The most common *Aspergillus* specie in respiratory samples of patients with cystic fibrosis is *A. fumigatus.* Reported prevalence rates for *A. fumigatus,* based on sputum cultures, range from 10% to 57% in patients with cystic fibrosis. Culture from a clinical sample is one of the parameters for diagnosis of fungal infection. It typically takes 100-120 h for identification of *Aspergillus* in a clinical sample too long for early treatment. Last studies *have* reported that MALDI-TOF demonstrates the feasibility by the use of a standardized procedure for the identification of *Aspergillus* clinical isolates, including cryptic species, grown either on solid or liquid media. Despite the good results, to date, MALDI-TOF is not widely used to identify *Aspergillus* spp. also because it is still necessary the isolation in culture of the microorganism.

Objectives. Identification and characterization of *Aspergillus* extracellular proteins in sputum, bronchoalveolar lavage fluid using MALDI-TOF for a rapid identification of *Aspergillus* infections.

Preliminary and expected results. It was performed characterization and evaluation of the quantity of production of exoproteins from different reference strain of *Aspergillus fumigatus, Aspergillus flavus, Aspergillus niger, Aspergillus terreus* growth in different cultural conditions. 202 sputum sample and 6 samples of bronchoalveolar lavage from patient with cystic fibrosis were recruited to the study. 2,8% of patients had pulmonary aspergillosis. It was compared the results of electrophoresis of sputum, bronchoalveolar lavage fluid and Aspergillus's cultural fluid.

Future perspectives. It will be demonstrate the usefulness of the new extracellular proteins database in MALDI-TOF MS by the use of procedure for the identification of proteins from *Aspergillus* from sputum, bronchoalveolar lavage.

TARGETED ANTIFUNGAL PROPHYLAXIS PROTOCOL IN LUNG TRANSPLANT RECIPIENTS: A PROSPECTIVE OBSERVATIONAL STUDY

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Background. Lung transplant recipients present a significant risk of fungal infections, mostly due to *Aspergillus spp* but also to *Candida spp*, *Cryptococcus spp* and more rare fungi. Bronchial anastomosis is susceptible to severe fungal infections leading to necrosis, stenosis and dehiscence. Universal prophylaxis is widely used worldwide but no randomized clinical trial has proven its efficacy. A methanalysis of 22 retrospective and observational studies showed no statistically significant difference in fungal infections and colonizations. Anothere methanalysis which included only comparative studies found that universal prophylaxis was associated with reductions in the incidence of fungal infections. The studies included in the methanalysis were conducted in a very large temporal period so it's difficult to compare such populations with different surgical and anesthesiological approaches. In patients receiving antifungal prophylaxis. The American Society of Transplantation (AST) guidelines suggest to use prophylaxis only in the presence of the following risk factors: *Aspergillus spp* pre- and post-transplant colonization (first year after transplant), *Aspergillus spp* colonization after CMV infection, alemtuzumab or Anti-Thymoglobulin (ATG) use, single lung transplant, rejection and augmented immune suppression, hypogammaglobulinemia. Since 2018 universal prophylaxis is no more considered the standard of care at Policlinico Umberto I and targeted prophylaxis is considered in the presence of one or more risk factors.

Aims. The aim of the study is to evaluate, in the lung transplant recipients population of Policlinico Umberto I, the impact of the antifungal prophylaxis strategy change in terms of: incidence of fungal infections, incidence of infections due to resistant fungi (es. *Scedosporium prolificans*, *Aspergillus calidoustus*, *Zygomycetes*, *Saprochaete spp*, etc) incidence of anastomosis complications, incidence of acute cellular rejection, use of antifungals (defined daily dose/1000 days/patient), antifungal hospital expense.

Expected results. We expect to observe: reduction of the use of antifungals, reduction of resistant fungi infections, reduction of antifungal expense.

Future perspectives. Comparison with the previous period when at Policlinico Umberto I universal prophylaxis was the standard of care (before 2018) will give us a definite answer of whether targeted antifungal prophylaxis is a valid option also at an "institution level".

CYTOMEGALOVIRUS REACTIVATION IN MULTIPLE SCLEROSIS PATIENTS ON DISEASE-MODIFYING TREATMENTS: IMPLICATIONS FOR NK CELL REPERTOIRE

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Background. Disease-Modifying Drugs (DMD) have radically changed the treatment of Multiple Sclerosis (MS), an autoimmune demyelinating disease of the central nervous system. DMD are either immunomodulatory and/or immunosuppressive and may carry a risk of viral infections or pre-existing latent reactivation, introducing new challenges in the care of MS patients. Recently ocrelizumab, an anti-CD20 monoclonal antibody that target B-cells has been approved for treatment of the progressive form of MS. However, as other DMD, ocrelizumab may increase the risk of Cytomegalovirus (CMV) reactivation. CMV is a herpesvirus widespread among human population, which is major cause of morbidity and mortality in immunocompromised hosts. CMV cause dynamic changes in the host immune system specifically in the Natural Killer (NK) subset. Several studies have reported that CMV is closely associated with the expansion of adaptive or memory-like NK-cell subsets (NKG2C+) with enhanced cytotoxic activity and immunoregolatory properties. This mature NK cells expansion is the hallmark of CMV infection and as reported, may exert a beneficial influence on MS clinical outcome.

Aims. The aim of the study is to evaluate the CMV reactivation risk through serological and molecular analysis in a cohort of MS patients under ocrelizumab treatment with a follow up for at least 24-month. Moreover, in order to identify early immunological markers of CMV reactivation, the relationship between CMV and NK cells will be investigated.

Expected results. This study would provide data on CMV risk reactivation of MS patients under ocrelizumab treatment and a better understanding of chronic CMV infection and immune system, especially focusing on the NK cell subset.

Future perspectives. CMV reactivation is one of most serious opportunistic infections under ocrelizumab treatment and the stratification of patients with a highest risk of reactivation is a crucial point to reduce the CMV related morbidity. This study might open new perspectives on the interaction between CMV and the immune system in MS.

EVALUATION OF THE IMPACT OF LONG LASTING INSECTICIDAL NETS (LLINS) ON MALARIA TRANSMISSION IN BURKINA FASO

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Background. Malaria is the first parasitic disease in the world for mortality and morbidity, recording the highest prevalence in sub-Saharan Africa with about 445.000 deaths and 2 million of new cases every year. LLINs are among the most effective strategies in malaria control. LLIN three-year distribution campaigns, recommended by the WHO, prevented 68% of the malaria cases in Africa, thanks to the combination of physical barrier and insecticidal activity against vectors. Despite this success, the effectiveness of LLINs in sub-Saharan Africa seems to be heterogeneous, since in some hyperendemic countries like Burkina Faso (where the LLIN reached 70%) the malaria incidence and the entomological infection rates are still very high. According to this scenario, from an entomological survey conducted in the rural village of Goden (Burkina Faso) in 2011 - i.e one year after the first LLINs distribution campaign - we detected unexpected high *Plasmodium* Sporozoite Rates (SR) of 7.1% in malaria vectors. This suggests a partial protective effect of LLINs in reducing transmission at population level in this area.

Objectives: we aim to evaluate the impact of LLINs on malaria transmission in Burkina Faso, taking the opportunity of a new distribution of nets in 2019 considering two areas differing for climate and vector species composition: Goden and Banfora. To this purpose, through the period 2019-2021, several endpoints will be monitored in the villages: entomological parameters (SR, human biting rates, insecticide resistance), local malaria clinical information and bednet physic conditions. Moreover, a systematic review will be conducted in order to investigate, at larger scale, possible correlation between malaria annual incidence and the performance of different LLIN brands according to their local usage in the country.

Preliminary and expected results. Data on mosquitoes collected in 2015 in Goden shows a rate of 1.5 infective bites/person/night both inside and outside houses, confirming partial protective effect of LLINs. Thus, the three-year entomological survey planned in two representative settings, as well as the information gathered from meta-analysis on different LLIN brands distributed in the country, will allow to measure the LLIN protective effect at individual and community level and to point out possible limits in durability (physical integrity, wash resistance, insecticide content) of LLINs used in Burkina Faso.

Future perspectives. This study could help to enlighten the reasons of LLINs reduced efficacy in Burkina Faso and possibly in other countries of sub-Saharan Africa where this tool seems to be ineffective, ultimately adding information of major importance in the planning of appropriate country-based malaria control strategies.

SEDENTARINESS AS A FRAILTY PREDICTOR: EXPERIMENTING THE PASE (PHYSICAL ACTIVITY SCALE FOR THE ELDERLY) AS A POPULATION SCREENING TOOL TO IDENTIFY THE RISK OF FRAILTY

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Background. The WHO program "Healthy and Active Aging" confirms the need to implement policies and strategies to contain economic and social costs in aging societies. This can be achieved through interventions aiming to delay the condition of frailty in elderly, to prevent a greater vulnerability to adverse health events and the risk of disability. The European Join Action "Advantage" on Frailty Prevention aims to identify the essential elements to define operational fragility, to develop a method to screen frailty in the Community and to indicate the most effective and feasible approaches for frailty prevention.

Objectives. This project aims to develop a tool to identify the elderly with low level of physical activity, one of the most significant predictors of frailty.

Preliminary and expected results. The purpose is to experiment the PASE "Physical Activity Scale for the Elderly" (an internationally validated instrument for measuring AF levels in the elderly) in a community context.

Health and social workers from 3 Italian Regions are involved in the following actions:

- enrollment of a cohort of over 64-year-olds with low levels of AF, measured through the PASE;
- promotion of physical activity and evaluation of PASE over time;
- final evaluation of PASE, perceived health and quality of life.

The first prototype of a smartphone App was developed, in order to help healthcare workers to estimate the PASE score; a training was given to the professionals involved.

Future perspectives. The future objective is to facilitate clinicians and public health operators to monitor sedentariness and to promote active aging among over-64 years old people. This is desirable in order to develop targeted programs for physical activity in those groups which are at major risk of frailty.

EXPOSURE EVALUATION OF THE POPULATION TO THE ATMOSPHERIC PARTICULATE BY SPATIAL MAPPING OF THE SOURCES CONTRIBUTIONS

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Objectives. The purpose of this study is to elaborate a new experimental procedure to assess the exposure of the population to atmospheric particulate by using innovative methods of spatial mapping of the sources contributions using the Terni area as a study area. Terni is situated in an intramountain depression where the PM is influenced by some important sources of PM (vehicular traffic, domestic heating, a power plant for waste treatment, a steel plant) it is ideal for the mapping of atmospheric pollutants being characterized by a poor reshuffling of the low atmosphere and by a different location of the main emission sources.

Expected results. An innovative methodology was used for taking field samples. The collection of PM2.5 and PM10 samples was performed by innovative low-flow self-powered samplers (Smart Sampler, by FAI Instruments), which work at a very low temporal resolution (30-40 days), in order to consider them representative of the data obtained without increasing too muchthe monitoring costs. Thanks to the low costs, the use of these systems allows the development of monitoring networks with high spatial resolution, thus obtaining a realistic mapping of the concentrations of PM and of the chemical compounds it contains. The analysis of the trace components (heavy metals and semi-metals, and polycyclic aromatic hydrocarbons, IPA) makes it possible to have additional information available on the PM emissive sources. The identification, by chemical characterization, of the species present in the traces, together with the determination of the macro-components of the PM will allow the generation of databases, which may have important dimensions both for spatial extension (regional scale) and temporal (annual), and for variety of chemical components (macro and trace) determined. The processing of spatial mapping data of chemical components is in progress. Calculations explain how each source category influences selectively each chemical component determined in the PM.

Future perspectives. The results obtained proved the efficiency of the new experimental procedure elaborated for the evaluation of the spatial variability of PM10 and its chemical components through the acquisition of spatially resolved data. In particular, the innovative smart samplers, used for the first time in this campaign, allowed to build an extended and extensive monitoring network with low associated costs which allowed to represent the different emission source contributes to total PM10 in the monitored area. The study will also be extended to the monitoring of biological samples (urine, hair, nails) taken from subjects residing in the study areas, in order to experimentally correlate the concentrations measured with exposure to atmospheric pollution.

ASSESSING GENETIC SERVICES FROM PATIENT'S PERSPECTIVE: A PATIENT REPORTED OUTCOME STUDY

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Background. The advances in genomics and related applications are promising a new era of personalized medicine, where medical decisions are tailored to an individual's characteristics, including the patient's genetic profile. This transformation especially concerns common chronic disorders, such as cancer, where genetic services have become part of clinical and public health practice. Since the interventions offered in clinical genetic services, i.e. genetic testing and counseling, are unlikely to directly improve health status measures (e.g. mortality and morbidity), assessing the value of such services is problematic.

Objectives. The project aims to assess clinical genetic services for Hereditary Breast and Ovarian Cancer (HBOC) using Patient Reported Outcomes (PROs), i.e. patients' subjective outcomes directly attributable to genetic services. PROs are usually collected through self-completion questionnaires aimed to assess whether genetic counseling has achieved its goals from the patient perspective. The specific objectives of the project are: identifying existing validated PRO measures; choosing the best tool to collect PROs; realize a PRO study in a sample of Italian HBOC clinical genetic services.

Expected results. To identify existing validated PRO measures and explore the best ways to conduct a PRO study, a systematic review of published PRO studies set in HBOC genetic services and focused on standard genetic counseling was performed. The systematic search identified ten surveys from various countries (USA n=5; Europa n=6), published between 2000 and 2018, mainly conducted in teaching hospitals or in cancer research and treatment institutes (n=9). The majority assess pre-test counseling (n=6) with diagnostic or predictive purpose. The most frequently measured outcomes are patient satisfaction (n=9), adherence to recommended preventive interventions (n=3), information sharing with relatives (n=3); disease risk perception (n=2), and psychosocial distress (n=2). Six studies adopted standardized PROs collection tools: the most common were the Genetic Counseling Satisfaction Scale and the Hospital Anxiety and Depression Scale. Questionnaires were mainly administered by post, soon after genetic counseling or up to seven years later.

Future perspectives. The study will point out the main critical issues of the involved services from a patient perspective and provide important elements to improve the quality and the patient-centeredness of HBOC genetic services. PROs are expected to be increasingly used as a measure of performance in order to drive the changes in how clinical genetic services, and healthcare in general, are organized, delivered and founded. Emerging information and communication technologies will help this process by making it easier collecting patient data.

ANISAKIS AND ALLERGY RISK IN WORKERS OF THE FISHING INDUSTRY

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Background. Exposure to biological agents (microorganisms, cell cultures and endoparasites) can cause diseases of infectious, allergic, toxic and carcinogenic nature. The allergy risk of biological origin may be present in many work environments, even if it is often underestimated and undervalued. Among the agents able to create awareness, the parasitic nematodes of the genus *Anisakis* have been recognized by the European Food Safety Authority (EFSA). The problem of allergy to *Anisakis* in the seafood business sector is considered an emerging risk and risk knowledge by operators of potentially exposed business sector is poor, as well as the application of practices / prevention and protection procedures in the workplace for risk management.

Objective. This project starts from the lack of knowledge on the *Anisakis*-driven allergy phenomenon in workers and from the insufficient reliability of the immunological screening methods so far available. The general objective of the project is the use of a multidisciplinary approach, starting from administration of clinical-cognitive-anamnestic questionnaires to the subjects recruited up to the study of potentially allergenic molecules.

Expected results. The study will contribute to improve the identification, knowledge and quantification of occupational allergy of parasitic origin within workers in fisheries; it is aimed to propose an operational protocol of assessment/monitoring and knowledge of the biological hazard that can cause work-related allergic diseases and disorders among workers in the fishing industry; it will improve the knowledge of experts in the risk management and help to develop "best practices" for workplace prevention. The preventive part will be coupled with an experimental content concerning the systematic study of the allergenic potential of the molecules available in the reference database. These will be used to develop ad hoc serological tests to be used on sera from allergic, exposed and unexposed subject.

Future perspectives. The results could help to develop health strategies for the protection of workers by policy makers and experts. Furthermore, the screening of potentially useful molecules to highlight exposure to *Anisakis* antigens could contribute to the development of early-warning innovative methods in order to improve the diagnostic and clinical management of parasitic allergies with the broader and more ambitious aim of providing tools for the differential diagnosis between food-borne and parasitic allergies.

STUDY OF THE KINETICS BIOTRANSFORMATION OF PESTICIDES AND NATURAL TOXINS FOR THE IDENTIFICATION OF EXPOSURE AND SUSCEPTIBILITY MARKERS AND POSSIBLE GROUPS OF POPULATION AT GREATEST RISK

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Background: We are daily exposed to many xenobiotics, as natural toxins or pesticides, via the environment, water and food. They can be toxic and tend to accumulate in adipose tissue and membranes, being generally lipophilic substances. As a defence mechanism, organisms promote their excretion, biotransforming them to more hydrophilic compounds through reactions catalysed by specific enzymes as Glutathione-S-Transferases (GSTs) or Cytochromes P450 (CYPs) characterized by different polymorphic isoforms.

Objectives. i) Characterization of the metabolic pathway of natural toxins, as Microcystins (MCs), and organophosphate pesticides (OPs); ii) Identification of the human GSTs or CYPs involved in metabolism suggestive of group of population more susceptible to the toxic effects due to genetic polymorphism; iii) Characterization of new biomarkers of exposure. This study will be carried out applying an integrated approach using human recombinant enzymes, human liver microsomes and cytosols and advanced analytical techniques.

Preliminary and expected results: The study started with the characterization of the detoxification reaction of three variants of MCs (LW, YR and LF), hepatotoxic and tumor promoters compounds. They are >200 congeners with different in vivo toxicity. The key event in their mechanism of toxicity, the in vitro inhibition potency of protein phosphatase, is comparable; therefore, the toxicokinetic of detoxification, mediated by the GSH conjugation, seems to be the critical point to explain the MC congener-dependent toxicity. The variants, such as MC-LW, YR and LF, having hydrophobic amino acids (e.g. tyrosine, tryptophan) may be more cell permeable than other MCs and also the detoxification reaction could be dependent on lipophilicity. At first, the logPow of 5 MC congeners has been determined, using the OECD guideline 117, and the ranking from the most lipophilic is: MC-LF>LW>LR>YR>RR. Moreover we have calculate the kinetics parameters (Vmax, Km and Cli) of MC-LW and YR and results indicate that the efficiencies of recombinant GSTs used are quite similar; the highest Cli were shown by GSTP1 and A1 (the most abundant in the liver) for MC-LW and P1=O1>A1 for MC-YR.

Future perspectives: This work is a part of an EU project financed by EFSA aimed to modeling the kinetics variability to predict the dynamic variability, our data will be used as an input for PBPK models. As next step OPs will be studied as well as other xenobiotics of toxicological interest.

ASSESSMENT OF GAS DISTRIBUTION IN ADVANCED DECOMPOSED BODIES BY POST-MORTEM COMPUTED TOMOGRAPHY (PMCT)

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Background. Decomposition represents a real challenge in forensic pathology because can impressively alter the appearance of the bodies, significantly increasing the risk of bias and leading to misinterpretation of the autopsy findings. Vascular and intra-parenchymatous gas collection is a hallmark of decomposition. In this context, PMCT represents an accurate procedure, allowing to detect gas in small amounts and distinguish between normal putrefactive gas and pathologic gas collections (air embolism, pneumothorax or pneumoperitoneum).

Methods. Ten forensic cases (8 males, 2 females) have been selected. The Post-Mortem Interval (PMI) ranged from seven to 887 days. All the bodies were PMCT-scanned prior to autopsy (Somatom® Sensation Cardiac 64-slice scanner, Siemens) according to a standardized scanning protocol. PMCT-data were transferred to a workstation for post-processing images reconstruction and were finally analyzed using a viewing software (OsiriX® v.5.8.2 32-bit, Pixmeo). The internal putrefactive state was determined using the Radiological Alteration Index (RAI), determined by PMCT in 7 selected sites, including the major vessels (left innominate vena and abdominal aorta), selected bones (vertebra L3), selected organs (heart cavities, liver parenchyma and vessels, and kidney parenchyma) and subcutaneous tissues and muscles (subcutaneous pectoral tissues), according a standardized protocol (grade of gas: 0, I, II, or III). After PMCT-scans, a complete conventional autopsy of each body was performed. The Grade of External Putrefaction (GEP) was assigned during the external examination of the bodies, according to a standardized classification (beginning, moderate, advanced, major, mummified). Causes of death were further investigated by histological, immunohistochemical and toxicological examinations.

Results. The analysis of the internal putrefactive state revealed that, in the 7 selected sites, the RAI was >78 in all bodies (interval 78-100, mean 92.6 ± 8.566 SD). In particular, the gas grade was >III in correspondence of the major vessels, heart cavities, vertebra L3 and subcutaneous pectoral tissues. Coherently, the GEP assessment at the cadaveric external examination revealed the presence of transformative phenomena from “major” to “mummified” in all bodies.

Conclusions. The combined use of GEP and RAI represents a useful tool in determining the external and internal putrefactive state, providing reliable data prior to autoptic investigation and supporting the forensic pathologist in the evaluation of cadaveric post-mortem changes.

NEW SYNTHETIC OPIOIDS: DEVELOPMENT OF ANALYTICAL METHODS FOR THEIR CHARACTERIZATION AND DETERMINATION BY MEANS (U) HPLC-HRMS/MS

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Background. In recent years, the synthesis and introduction into the illicit market of NPS has reached alarming levels. More than 540 compounds have been identified by the EMCDDA. In this context, it is of significant importance to have the right tools to identify the most recent NPS and verify their consumption. Synthetic opioids deserve special attention, in particular fentanyl derivatives that in 2018 covered more than 70% of the world demand for opioids, with thousands of fatal events in USA.

Objectives. The objective of the project involves the identification of the main metabolites of NPS and the development of innovative, fast and simple analytical methods, for the determination of these compounds in the different biological matrices, with a focus on synthetic opioids.

Expected results. An HPLC-HRMS/MS method has been developed that allows the separation, identification and quantification of over 10 synthetic opioids, including NPS and fentanyl derivatives, in 14 minutes. It has been possible to characterize three fentanyl derivatives by means of HRMS; as a consequence, a report to the National Early Warning System regarding a new synthetic fentanyl derivative was provided. To date, a method of pretreatment of the oral fluid matrix has been developed using Solid Phase Extraction performed by Microextraction on Packed Sorbent (MEPS-C18). Through this technique, it was possible to effectively extract the analytes from the matrix, favoring their determination thanks to the high enrichment factor and the elimination of the matrix effect. In order to demonstrate its high versatility, the same technique will then be applied to the clean-up of plasma and urine matrices.

Future perspectives. We expect to be able to characterize NPSs in seizures and in biological matrices; in the latter case it will be necessary to perform in silico, in vitro and in vivo studies with the aim to identify the metabolic pathways and so discriminate the active use of the substance from a false positive; furthermore it is proposed to constantly expand the number of analytes that can be determined with the proposed methods. Clean-up methods will be develope for different biological matrices (such as hair, nails, sweat) to obtain a general picture of the consumption of synthetic opioids over time and to be able to make an effective contribution to the estimation of the real propagation of the NPS on the Italian illegal market.

CONSTRUCTION OF STATISTICAL-MATHEMATICAL MODELS FOR THE STUDY, CONTROL AND EVOLUTION OF THE SPREAD OF PATHOGENIC MOSQUITOES

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The presence of invasive mosquitoes in Italy, in particular *Aedes albopictus*, has had a significant impact on public health having caused the largest outbreak of arbovirosis on European soil. Currently, the estimate of the health risk is limited by the inability to predict the space-time distribution of the vectors. Therefore, the aim of this PhD project is to develop mathematical-statistical models to identify the spatio-temporal distribution of *Aedes albopictus* and *Aedes koreicus*, vectors of human and animal pathogens, and to evaluate the relative risk for public health. The project is divided into several phases: 1-statistical analysis of the data available in the Medical Entomology group of Sapienza and the Biodiversity and Molecular Ecology group of the Edmund Mach Foundation; 2-revision of the estimates obtained to evaluate their applicability in mechanistic models; 3-integration of statistical-mathematical models with field observations and laboratory estimates to objectively assess the health risk posed by the *Aedes* species. The final objective of the project is to contribute to national and regional health surveillance plans for arbovirosis by providing quantitative bases to establish the best monitoring strategies to identify and estimate the risk of viral transmission. In the first phase of the project, the analysis focused on data collected in 2016 by the Sapienza Medical Entomology group on the island of Procida to assess the reliability and robustness of the main monitoring methods for *Aedes albopictus.* The object of the study was the comparison between egg collections through ovitraps and adult mosquitoes through Human Landing Collection (HLC) also considering explanatory variables such as the presence of human guests or the type of territories. The results show, for adult mosquitoes, an association with the percentage of trees in a 20m buffer and a spatial correlation of 324m, while for eggs we can see an association with the percentage of bare soil in a 200m buffer and spatial correlation of 400m. The results allow us to infer how many traps to place in a territory to estimate the distribution of the vector and its relative abundance to evaluate possible hot-spots.

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