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XI Seminar - PhD Day

COVID-19: Facing a multi(face)phase pandemic

Virtual Meeting

Organized by the Italian National Institute of Health and

Sapienza University of Rome

September 17 and 24,

October 1 and 8, 2020

ABSTRACT BOOK

Edited by

I. Bellini, S. Buezo Montero, G. Civitelli, A. Di Rocco,

V. Perri, L. Besi, F.M. Damato, R. Tittarelli, G. Marchetti,

A. Di Pucchio and A. Mazzaccara

ISTITUTO SUPERIORE DI SANITÀ

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Edited by
Ilaria Bellini (a), Sara Buezo Montero (a), Giulia Civitelli (a),
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2020, xiii, 95 p. ISTISAN Congressi 20/C1

The 11th Seminar of PhD students in Infectious Diseases, Microbiology and Health Sciences has been delayed and will be carried out online due to the recent COVID-19 pandemic. Indeed, this tragical event, that has dramatically affected people's life all over the world, will be the core of the topics considered. The Seminar is scheduled in four days, each characterized by an in-depth analysis of topics related to the pandemic, such as the establishment of predictive models, the clinical, diagnostic and anatomopathological aspects, the effects of social distancing and the impact of the pandemic on the socially less-favoured people.

Key words: Pandemic; COVID-19; Microbiology, Infectious Diseases, Public Health, Social Medicine, Forensic Medicine

Istituto Superiore di Sanità

XI Seminario - PhD Day. COVID-19: affrontare una pandemia multifacciale. Incontro Virtuale. Organizzato dall'Istituto Superiore di Sanità e dalla Università Sapienza di Roma. 17 e 24 settembre, 1° e 8 ottobre 2020. Riassunti.

A cura di Ilaria Bellini, Sara Buezo Montero, Giulia Civitelli, Arianna Di Rocco, Valentina Perri, Livia Besi, Felice Marco Damato, Roberta Tittarelli, Giulia Marchetti, Alessandra Di Pucchio e Alfonso Mazzaccara

2020, xiii, 95 p. ISTISAN Congressi 20/C1 (in inglese)

L'undicesimo Seminario dei Dottorandi di Malattie infettive, microbiologia e sanità pubblica si svolge in ritardo e con modalità in remoto per la recente pandemia da COVID-19. Proprio questo evento, che ha modificato in maniera significativa la vita delle persone praticamente in tutto il mondo, è al centro degli argomenti trattati. Il Seminario si svolgerà in quattro sessioni, ognuna caratterizzata dall'approfondimento di temi legati alla pandemia, ovvero la costruzione di modelli predittivi, gli aspetti clinico-diagnostici e anatomico-patologici, gli effetti del distanziamento sociale e infine come la pandemia ha avuto effetti sulle popolazioni con disagio sociale.

Parole chiave: Pandemia, COVID-19, Microbiologia, Malattie Infettive, Sanità Pubblica, Medicina Sociale, Medicina Legale

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PROGRAMME

Thursday, September 17, 2020

- 8.30 Log into the platform
- 8.45 Preliminary welcome
Alfonso Mazzaccara
Training Office, Italian National Institute of Health, Rome, Italy
Anna Rita Vestri, Paolo Villari, Stefano D'Amelio
Department of Public Health and Infectious Diseases, Sapienza University of Rome,
Rome, Italy

Session 1

EPIDEMIOLOGICAL AND MATHEMATICAL MODELLING OF SARS-CoV-2 INFECTION

Chairpersons: Arianna Di Rocco, Ilaria Bellini

- 9.00 Lecture
Surveillance of COVID-19 in Italy
Patrizio Pezzotti
- 9.30 Lecture
Nowcasting the Italian epidemic outbreak of SARS-CoV-2
Alessio Farcomeni
- 10.00 Lecture
The study of COVID-19 in small municipalities and the problem of communicating scientific results to a large audience
Giovanna Jona Lasinio

10.30-13.30

PHD CANDIDATES' COMMUNICATIONS

Unexpected increase of myocardial extracellular volume fraction in low cardiovascular risk HIV patients: a new cardiovascular risk marker?
Cristian Borrazzo

Validation of a score system in the management of litigation related to healthcare-related infections. Applicability in the context of private health
Shima Gholamalishahi

Patient involvement in research: the role of cystic fibrosis patient organizations across Europe

Vittorio Gatto

The effect of physical activity on lifestyle and quality of life in patients with Alzheimer's disease

Luigi Graziano

Neurotoxic compounds in freshwater: a new rapid toolscreen with zebrafish embryo

Ines Lacchetti

Occurrence, distribution and ecology of Anopheles mosquitoes and risk of malaria re-emergence in Italy

Fabrizio Montarsi

Local policies for access to healthcare of migrants in Italy. A subset of indicators monitoring regional implementation of national law

Valentina Pettinicchio

Population risk assessment to the atmospheric particulate in Terni area by high spatial resolution mapping of the sources contributions

Eva Pietrantonio

Epidemiological study of HEV prevalence in patients suffering from Amyotrophic Lateral Sclerosis (ALS) or Chronic Inflammatory Demyelinating Polyneuropathy (CIPD)

Marco Rivano Capparuccia

COVID-19 control: lessons from the "Palazzo Pecile" outbreak in Rome

Annalisa Rosso

Identification of human cytochrome P450 isoforms in phosmet bioactivation and metabolic interactions with chlorpyrifos

Nicoletta Santori

E-Learning courses at Italian National Institute of Health: characteristic of dropout participants

Nordino Sulemane

Mathematical modelling of flying-mosquitoes dispersal: a PDE based approach

Chiara Virgillitto

Thursday, September 24, 2020

- 8.30 Log into the platform
- 8.45 Preliminary welcome
Anna Teresa Palamara, Claudio Maria Mastroianni, Stefano D'Amelio
Department of Public Health and Infectious Diseases, Sapienza University of Rome,
Rome, Italy

Session 2

CLINICAL AND IMMUNOLOGICAL FEATURES OF COVID-19

Chairpersons: Sara Buezo Montero, Valentina Perri

- 9.00 Lecture
Immune response to SARS-CoV-2: pros and cons
Andrea Cossarizza
- 9.30 Lecture
Phase I and entering the next phases of COVID-19: microbiological and public health aspects
Paola Stefanelli

10.30-13.30

PHD CANDIDATES' COMMUNICATIONS

In vitro study of the synergistic activity of n-acetylcysteine associated with β -lactam antibiotics against New Delhi metallo-beta-lactamase producing Enterobacteriaceae

Dania Al Ismail

Validation of human IgG response to Aedes salivary proteins as a novel markers of human exposure to Aedes albopictus

Sara Buezo Montero

Genotypic and phenotypic characterization of staphylococci from atopic dermatitis patients

Antonietta Lucia Conte

Personalised exercise training programme for HIV-infected patients: effects on exercise tolerance and immune activation

Marcello Di Paolo

Impact of chlamydia trachomatis on human Sertoli cells in the etiopathogenesis of male infertility

Simone Filardo

Impact of antiretroviral therapy on gut CD4 T cells activation: differences between naïve and long-term treated HIV-1 infected patients

Giuseppe Pietro Innocenti

Glia-neuron crosstalk during-HSV-1 infection

Olga Kolesova

Evolution of fibrosis indexes, liver function and carbohydrate and lipid metabolism in patients with chronic hepatitis C who have eradicated the infection

Simone Lanini

Psycosexual health and systemic, mucosal immune activation in HIV-infected art suppressed and uninfected women: evaluation of biomarkers and environmental stimuli

Parni Nijhawan

Studying of extracellular proteins of Aspergillus

Anastasia Orekhova

Ureaplasma spp Infection in Solid Organ Transplant: Prospective Clinical Study

Paolo Pavone

Infectious risk in Ocrelizumab-treated multiple sclerosis patients

Valentina Perri

Limited impact of Long Lasting Insecticide Treated Nets (LLINs) on malaria transmission in a rural village of Burkina Faso: the role of mosquito behavioral plasticity

Eleonora Perugini

First draft of a miRNA catalogue from Anisakis pegreffii infective third-stage larvae and exosomes-enriched fraction

Antonella Pizzarelli

Lactoferrin against inflammatory and iron disorders in different infection models

Luigi Rosa

Gram-negative septic thrombosis in critically ill patients: a retrospective case-control study

Martina Spaziante

The burden of infections in severely injured trauma patients admitted to the intensive care unit

Tiziana Tieghi

Characterization of invasive Neisseria meningitidis serogroup C isolated in Italy

Paola Vacca

Thursday, October 1, 2020

- 8.30 Log into the platform
- 8.45 Preliminary welcome
Ciro Villani
Department of Human anatomy, Histology, Forensic medicine and Orthopedics,
Sapienza University of Rome, Rome, Italy
Vittorio Fineschi
Department Section of Medical Law, Sapienza University of Rome,
Rome, Italy
Stefano D'Amelio
Department of Public Health and Infectious Diseases, Sapienza University of Rome,
Rome, Italy

Session 3

COVID-19 LEGAL ISSUES

Chairpersons: Livia Besi, Felice Marco Damato, Roberta Tittarelli

- 9.00 Lecture
*Science that lights up the dark: the contribution of Pope John XXIII Hospital
in the battle against COVID-19*
Andrea Gianatti
- 9.30 Lecture
*Hospital emergency assistance procedures for victims of violence and abuse:
the experience of Sant'Andrea Hospital before and after lockdown*
Simona Abate

10.00-13.00

PHD CANDIDATES' COMMUNICATIONS

*Caffeine consumption in professional, amateur athletes and cadaver,
as representative of general population: toxicological evidences,
co-use of other substances and potential mechanisms of damage*
Simone Cappelletti

Effect-based methods for monitoring and assessment of aquatic ecosystems
Mario Carere

*Correlations between Rorschach and WAIS-IV in subjects
with intellectual disability*
Felice Marco Damato

Review about application of law 24/2017 (Gelli) during the first three years since its entry in force

Umberto De Gennaro

Multiple implications of Post Mortem Computed Tomography (PMCT) in the forensic approach to charred bodies

Massimiliano Dell'Aquila

Patient safety: claims analysis and clinical risk management

Mariantonia Di Sanzo

Regulation of miRNAs as a new tool for cutaneous vitality lesions demonstration in ligature marks in deaths by hanging

Aniello Maiese

Exhumation of unidentified bodies at the cemetery of Rome: ongoing identification

Chantal Milani

Sudden Cardiac Death (SCD): looking for predictive genetic markers

Angelo Montana

Post-Mortem Cardiac-Magnetic Resonance (PMCMR): a novel diagnostic tool in Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)

Alessandro Santurro

The fear of the unknown: the impact of COVID-19 lockdown on the use of legal and illegal psychotropic substances

Roberta Tittarelli

Toxicological and legal aspects on road safety

Fabio Vaiano

Thursday, October 8, 2020

8.30 Log into the platform

8.45 Preliminary welcome

Maurizio Marceca, Paolo Villari, Stefano D'Amelio

Department of Public Health and Infectious Diseases Department, Sapienza University of Rome, Rome, Italy

Session 4

THE IMPACT OF THE COVID-19 PANDEMIC ON HUMAN RIGHTS

Chairpersons: Giulia Civitelli, Giulia Marchetti

9.00 Lecture
Diseguaglianze in salute e pandemia da SARS-CoV-2
Giuseppe Costa

9.30 Lecture
Tutela della salute dei migranti e pandemia da SARS-CoV-2
Salvatore Geraci

10.00-13.00

PhD CANDIDATES' COMMUNICATIONS

Gender differences and occupational factors for the risk of obesity in the Italian working population
Giovanna Adamo

Integrating climate and environment public datasets in surveillance for early warning
Laura Amato

Global health education in Italian universities
Giulia Civitelli

Mass spectrometric specific detection of Polycyclic Aromatic Hydrocarbons (PAH) in GC/MS-NCI without using auxiliary ionization gas. A method for the analytical determination of PAH correlated with their carcinogenicity
Ettore Guerriero

Immunization challenges targeting newly arrived migrants
Giulia Marchetti

National monitoring system for patient safety in Italy, consensus based approach and data sources integration
Daniele Mipatrini

Implementing health technology assessment for genomic technologies in Italy: network, pathways and methodology
Erica Pitini

Assessment of the social impact of subjective stress in different work populations compared
Carmina Sacco

*Determinants of adherence to ART in HIV+ women enrolled in PMTCT program
in west and north regions of Cameroon*

Armand Tiotsia Tsapi

*New synthetic opioids: development of analytical methods for their
characterization and quantification by means of (U) HPLC-HRMS/MS*

Flaminia Vincenti

*The evaluation of palliative care and the needs in primary health care
in the city of Vlore*

Juljana Xhindoli

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 11th Seminar of PhD students has been delayed and will be carried out online due to the recent COVID-19 pandemic. Indeed, this tragical event, that has dramatically affected people's life all over the world, will be the core of the topics considered. The Seminar is scheduled in four days, each characterized by an in-depth analysis of topics related to the pandemic, such as the establishment of predictive models, the clinical, diagnostic and anatomopathological aspects, the effects of social distancing and the impact of the pandemic on the socially less-favoured people.

As usual, the PhD students of the third year will present orally their results. In this edition, students at the second year will present their studies as a brief communication, while the abstracts of first year students' studies are included in the "New research topics" section of this abstract book.

This will permit to a wide audience to get in touch with the most updated researches in the field.

The Scientific Staff

*Ilaria Bellini, Sara Buezo Montero,
Giulia Civitelli, Arianna Di Rocco,
Valentina Perri, Livia Besi, Felice
Marco Damato, Roberta Tittarelli,
Giulia Marchetti, Alessandra Di
Pucchio, Alfonso Mazzaccara*

Session I

**Epidemiological and mathematical modelling
of SARS-CoV-2 infection**

Chairpersons

Arianna Di Rocco, Ilaria Bellini

UNEXPECTED INCREASE OF MYOCARDIAL EXTRACELLULAR VOLUME FRACTION IN LOW CARDIOVASCULAR RISK HIV PATIENTS: A NEW CARDIOVASCULAR RISK MARKER?

Cristian Borrazzo (a), Gabriella d’Ettorre (a), Claudio Iacopo Carbone (b), Claudio Maria Mastroianni (a)

(a) *Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy*

(b) *Department of Radiological, Oncological and Pathological Sciences, Sapienza University of Rome, Rome, Italy*

Background. People Living With HIV (PLWH) are prone to develop sub-clinical Cardiovascular (CV) disease, despite the effectiveness of combined Antiretroviral Therapy (cART). Algorithms developed to predict CV risk in the general population could be inaccurate when applied to PLWH. myocardial Extra-Cellular Matrix (ECM) expansion, measured by computed tomography, has been associated with an increased CV vulnerability in HIV-negative population. Measurement of Myocardial Extra-Cellular Volume (ECV) by computed tomography or magnetic resonance, is considered a useful surrogate for clinical evaluation of ECM expansion. In the present study, we aimed to determine the extent of cardiovascular involvement in asymptomatic HIV-infected patients with the use of a comprehensive Cardiac Computed Tomography (CCT) approach.

Methods. In the present study, ECV in low atherosclerotic CV risk PLWH was compared with ECV of age and gender matched HIV- individuals. 53 asymptomatic HIV+ individuals (45 males, age 48 (42.5-48) years) on effective cART (CD4+ cell count: 450 cells/ μ L (IQR: 328-750); plasma HIV RNA: <37 copies/ml in all subjects) and 18 age and gender matched controls (14 males, age 55 (44.5-56) years) were retrospectively enrolled. All participants underwent CCT protocol to obtain native and postcontrast Hounsfield unit values of blood and myocardium, ECM was calculated accordingly.

Results. The ECV was significantly higher in HIV+ patients than in the control group (ECV: 31% (IQR: 28%-31%) vs 27.4% (IQR: 25%-28%), $p < 0.001$). The duration of cART (standardized $\beta = 0.56$ (0.33-0.95), $p = 0.014$) and the years of exposure to HIV infection (standardized $\beta = 0.53$ (0.4-0.92), $p < 0.001$), were positively and strongly associated with ECV values. Differences in ECV ($p < 0.001$) were also observed in regard to the duration of exposure to cART (<5 years, 5-10 years and >10 years). Moreover, ECV was independently associated with age of participants (standardized $\beta = 0.42$ (0.33-0.89), $p = 0.084$).

Conclusion. HIV infection and exposure to antiretrovirals play a detrimental role on ECV expansion. An increase in ECV indicates ECM expansion, which has been associated to a higher CV risk in the general population. The non-invasive evaluation of ECM through ECV could represent an important tool to further understand the relationship between HIV infection, cardiac pathophysiology and the increased CV risk observed in PLWH.

VALIDATION OF A SCORE SYSTEM IN THE MANAGEMENT OF LITIGATION RELATED TO HEALTHCARE-RELATED INFECTIONS. APPLICABILITY IN THE CONTEXT OF PRIVATE HEALTH

Vittorio Gatto, Paola Frati

Department Anatomical, Histological, Forensic and Orthopedics Sciences, Sapienza University of Rome, Rome, Italy

Background. Healthcare associated infections (HEI) represent a very important challenge for healthcare facilities since in recent years they are becoming increasingly important in economic terms with direct and indirect costs as well as socially considering the possible deaths, the need for long-term care and for the possible more or less serious disabilities in which they can hesitate.

Methods. Malpractice claims received at a some of accredited private healthcare facilities in southern Italy were analyzed. Subsequently, claims for compensation related to healthcare-related infections were selected and a medico-legal evaluation was carried out to identify the inadequacies of the healthcare path. The degree of losing was determined using the ALEA (Advanced Loss Eventuality Assessment) score, a 14-element scoring system designed specifically for HEI. For some cases that have already reached an advanced stage of judgment (final CTU or sentence), the congruence between the judicial outcome and the estimate of the risk of losing has previously been verified.

Results. The partial data that emerge confirms a moderate economic weight of healthcare-related infections even in the context of accredited private health care despite the presence of numbers that in some cases are significantly lower than the national average. The emerging data confirm the ability of the ALEA score to predict the judicial outcome of the accident with a good approximation.

Conclusions: The analysis of data relating to healthcare associated infection can be a valuable aid in identifying assistance and/or organizational deficiencies. However, the analysis of the incidence rates of these events cannot be exempted from the comparison with the amount of health services provided, nor from the socio-environmental context in which the event occurs. In this context, a predictive score can facilitate health structures in the management of claims concerning ICA, allowing to identify those potentially more at risk of losing and for which significant economic savings could be configured if closed in an out-of-court context, thus avoiding any increase in expenses associated with the judicial process.

THE EFFECT OF PHYSICAL ACTIVITY ON LIFESTYLE AND QUALITY OF LIFE IN PATIENTS WITH ALZHEIMER'S DISEASE

Shima Gholamalishahi, Giuseppe La Torre

Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

Background. Chronic brain disorders are associated with reduced Quality of Life (QoL), high prevalence of low mood and depression, stress sensitivity and cognitive dysfunction. Alzheimer's Disease (AD) is an irreversible and progressive neurodegenerative disorder that slowly destroys memory and is the most prevalent form of dementia in the elderly population. AD affects approximately 0.6% of the world population and occurs in 6% of people over the age of 65 years. As the average life expectancy continues to increase, this percentage is expected to increase to 1.2% of the world's population by the year 2050. Among the many preventive factors being studied, exercise is thought to play a vital role in not only preventing the pre-clinical stage of AD even slowing the clinical progression of AD. Therefore, present study aimed to investigate the effect of physical activity on lifestyle and quality of life in patients with AD.

Methods. The study will be a case-control investigating the association between physical activity with QoL and lifestyle behaviors in patients with AD. The case-control study is the first phase and involves collecting data and analyzing quantitative data. The study will be carried out using collected data of Italian, Iran, and Russia elderly patients with AD. Participant must over 60 years and will be selected according to the sample - size calculations for a case-control study and separate two groups include patients (AD) and control (friends or neighbors of the case-group members).

Expected results. Physical activity reduces the risk for mortality and chronic diseases, and as a health promotion improve lifestyle, psychological factors as well as functional cognitive in adult and older people. We expect to contribute to the evidence concerning the positive association between physical activity with QoL, lifestyle behaviors in patients with AD.

Conclusions. The aim of this project to identify patients in a presymptomatic stage for early treatment to delay progressive cognitive decline and disease onset and to development of new diagnostic markers of Alzheimer's disease. 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 levels.

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

Luigi Graziano (a), Paolo Palange (b)

(a) Department of Maternal, Infantile and Urological Sciences, Sapienza University of Rome, Rome, Italy

(b) Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

Patients with Cystic Fibrosis (CF) are assuming an increasingly important role in providing their perspective on research priorities. The aim of this project is to provide an overview of the strategies, challenges and proposals among the European CF Patient Organizations (POs) for the active engagement of patients in research. In September 2019, an electronic survey was sent to members of 39 national CF POs. The main findings of this survey show that the topic of patient involvement in research is of great interest among European POs members. Information about ongoing trials is considered the most relevant example of patient active participation in research. The involvement of trained patients in the reviewing of study protocols is an important point according to 80% of respondents. A critical issue is the emphasis that respondents placed on in person events when asked to indicate initiatives useful to promote patient involvement in research. This could expose participants to the risk of cross infection.

Lastly, when asked about the type and level of engagement that would be important to promote only 10% answered “control” (patients are the driver of the research projects). This may indicate a need to provide a clear definition and demonstration of what patient involvement in research means.

The questionnaire made it possible to get a description of the initiatives taken for CF patient involvement in research across Europe. It appears that a gap could exist between high-income countries and low-income and middle-income countries in patients active participation in research. Comparing respondent and non-respondent POs nationality according to the gross national income it can be noted that the proportion of high income countries is higher among European PO members that responded to the survey (60%) than in the non-respondents group (29%). This different attention to the problem might indicate a diverse order of priorities due to differences of resources.

In conclusion, the active involvement of CF patients in research needs a great engagement of the entire CF community. It is important to further strengthen cooperation between POs, Scientific Societies, pharmaceutical companies and policy makers. New technologies can play an important role, promoting involvement while avoiding the risk of cross infections, but they may also increase inequalities as many people do not have access to these technology tools. So, it is important to implement flexible strategies which consider the specific characteristics that exist at national level across Europe.

NEUROTOXIC COMPOUNDS IN FRESHWATER: A NEW RAPID TOOLSCREEN WITH ZEBRAFISH EMBRYO

Ines Lacchetti, Laura Mancini

Ecosystem and Health Unit, Department of Environmental and Health, Italian National Institute of Health, Rome, Italy

Background. Thousands toxic substances daily reach aquatic environment, mainly deriving from industrial, urban and agricultural activity. Many of them exhibit neuroactive properties and they are considered an emerging issue for both human and environment health. The real impact of the exposure of neurotoxic contaminants on ecosystem is not yet much known but there are evidences that they can cause important changes in organism behaviour, furthermore also humans can be indirectly exposed to neurotoxicants through ingestion of fishery products and drinking waters. An improvement to bridge the gap of knowledge in this sector is needed and new standardized methods are required.

Methods. The aim of this study is to verify the feasibility and applicability of the coiling activity test with zebrafish embryo applied on environmental samples. Spontaneous movements of the tail in embryo occurred earlier at 17 h post-fertilization originate from a single neural circuit and they are influenced by contaminant exposure. The count of bursts and their intensity are important parameters of neurotoxic effect and specific software allows the rapid measurement of them. We applied the coiling activity test on different environmental samples in 24 well plates at different laboratory conditions in order to suggest a rapid operating protocol as a screening identification and cost effective test in the ecotoxicological assessment. In parallel we utilized the 96 hours Fish Embryo toxicity acute test (OECD, 236) to add more information on the samples and to verify the sensibility between two tests.

Results. Preliminary results highlight the increasing of burst numbers after 24 hours mainly correlated to the environmental samples with major acute toxicity obtained after four days.

Conclusions. The spontaneous tail movement in zebrafish is demonstrated to be a very powerful tool in eco-neurotoxicological studies as it provides in few hours important screening information on the presence of dangerous substances in ecosystem. This test could give also a valid contribute to increase the regulatory guidelines to identify neurotoxic risks in ecosystem.

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

Fabrizio Montarsi (a,b), Marco Pombi (b)

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Background. In Europe and Italy, after malaria eradication, the risk of autochthonous infection is currently considered low, but climate and habitat modifications may change this scenario. The aim of this study is to evaluate the current risk of re-introduction and emergence of autochthonous cases of malaria in North-East of Italy, where *Anopheles* vectors are still abundant, by collecting data useful to estimate the "malariogenic potential" such as occurrence, density and distribution of *Anopheles* mosquitoes, anthropophily and host choice.

Methods. An entomological surveillance was carried out in Veneto and Friuli Venezia Giulia regions (2018-2019) collecting adult mosquitoes by traps, resting catches, and larval dipping. The activity was performed in environments (urban, suburban and rural) potentially suitable for *An. maculipennis s.l.* species. Collected mosquitoes were morphologically identified and confirmed by molecular analysis (PCR on ITS-2) and sequencing. Anthropophily was evaluated by Human Landing Catches (HLC) in two selected rural sites known for the presence of *An. maculipennis s.l.* Host choice will be assessed by molecular blood meal analysis of engorged mosquitoes collected in all sites. Comparative trap performance in collecting *Anopheles* was also evaluated in two sites.

Results. So far, 75/90 (83.3%) sites monitored for adult mosquitoes were positive for *Anopheles* species. They were found mainly in rural-suburban sites as animal shelters (82.4%), warehouses (10.8%), abandoned dwellings (4.0%). In total, 2,318 adult *Anopheles* were collected, mostly belonging to *An. maculipennis* complex (98.8%). The highest density recorded was about 900 specimens/sampling. Preliminary PCR analysis performed on 437 *An. maculipennis s.l.* adults show the presence of *An. messeae s.l.* (70.0%), *An. maculipennis s.s.* (27.7%), and *An. atroparvus* (2.3%). *Anopheles* spp. larvae were found in 22/31 sites (71%), mainly in large artificial water containers (36.8%) and paddy fields (23.7%). Data on HLC and host preference are not processed yet.

Conclusions. Results obtained so far show that species of *An. maculipennis* complex are widespread in northeastern Italy but their occurrence is displayed in scattered foci. In particular, *An. messeae* is the most common species, occurring mainly around Venice lagoon and Po River, while *An. atroparvus* was found only in Verona province. Despite the historical main malaria vector in this area (*An. sacharovi*) seems to be absent, our findings show that secondary malaria vectors are still present and locally abundant in some area of Delta Po River and Verona province, reaching higher density during the late summer.

LOCAL POLICIES FOR ACCESS TO HEALTHCARE OF MIGRANTS IN ITALY. A SUBSET OF INDICATORS MONITORING REGIONAL IMPLEMENTATION OF NATIONAL LAW

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Background. According to the 2019 WHO report on the health of refugees and migrants in the WHO European Region, migrants, although enjoying better health on arrival, have higher risk to get sick over the years. This occurs partly because of the lack of access to health services: WHO stressed the importance of ensuring access to high quality health services, culturally and linguistically sensitive, and to care for an appropriate and careful monitoring. The project aims to design and to experience a subset of indicators to monitor the implementation, at local level, of the national law for health care of the migrant population (Law on Migration 286/1998, amended by Law No. 132 of 1 December 2018 and by Law No. 77 of 8 August 2019).

Methods. A panel of experts in migration medicine assigned a score to a series of migrants' health topics, in order to assess their "priority". Later, the main topics were submitted to the analysis of different multidisciplinary groups (jurists, doctors, etc.) which, through the World Cafè methodology, made different proposals for the gradation of the indicators. A value, from 0 to 3, has been assigned to each indicator on the basis of what is envisaged and implemented at local level for the topic considered. The proposals obtained were integrated by a commission made up of three researchers (the authors of the presented abstract), and a grid was created to be submitted again to the panel of experts, to start the experimentation. Furthermore, for each indicator, in order to allow a further assessment of congruence between the assigned value and the reality, it is required to send the official documentation to refer to.

Results. The panel of experts in migration medicine identified 12 main topics to be considered for monitoring, addressed in different regulatory sources or guidelines. These correspond to 12 summarizing indicators, registered also across different geographic boundaries and aimed to track progress over time. Monitoring has been currently carried out in 5 Italian Regions, three in northern Italy, one in the center and one in the south. 4 out of 5 regions fed the entire grid of indicators.

Conclusions. The monitoring activity was obviously affected by the emergency due to the COVID pandemic. It is hoped that the resumption of healthcare activities, together with the need to protect the health of the most fragile people, which the pandemic itself has put in the background, will renew the attention towards this project.

POPULATION RISK ASSESSMENT TO THE ATMOSPHERIC PARTICULATE IN TERNI AREA BY HIGH SPATIAL RESOLUTION MAPPING OF THE SOURCES CONTRIBUTIONS

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Background. The chemical characterization data of the atmospheric Particulate Matter (PM) and its components in Terni area outdoor environment allowed to calculate carcinogenic and non-carcinogenic risk associated with chemical species (mainly metals Cd, Cr, Cu, Fe, Mn, Ni, Pb, and Zn). Data were obtained during a previous extensive annual high resolution monitoring campaign in Terni area located in an intramontane depression influenced by some important sources of PM. Terni is particularly suitable for the study of atmospheric pollutants, being characterized by a poor mixing of the low atmosphere and by a different position of the main emissive sources.

Methods. The measurements carried out using innovative samplers for high spatial resolution monitoring of networks provided an experimental mapping for the entire year of realistic PM concentrations and the related components (due to different sources of vehicular traffic, home heating, a power plant for treatment waste, a steel plant). Data were analyzed to calculate carcinogenic and non-carcinogenic risks. The risk values were calculated through accredited algorithms of EPA methodologies (Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part F, Supplemental Guidance for Inhalation Risk Assessment) for carcinogenic and non-carcinogenic substances.

Results. The risks were calculated using EPA accredited algorithms (Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part F, Supplemental Guidance for Inhalation Risk Assessment methodologies). The non-carcinogenic risk values calculated on children show risk levels higher than EPA reference value in all sampling stations. The non-carcinogenic risk values calculated on the adult show risk levels higher than EPA reference value in few sampling stations. The carcinogenic risk values calculated on the entire population show risk levels higher than EPA reference value in two stations, in particular relating to RO and PR.

Conclusions. The defined methodology proved to be extremely effective for a realistic analysis of the distribution of the particulate matter, of its components according to the emission sources and the resident population and risk assessment. The results can be used to develop risk maps with high spatial resolution, which will form a solid basis for the interpretation of geo-referenced epidemiological data and the risk maps will allow a predictive risk assessment of the population exposed in an area. In Terni area the most important emissive sources have persisted in this area for several years, causing a long-term exposure for the population.

EPIDEMIOLOGICAL STUDY OF HEV PREVALENCE IN PATIENTS SUFFERING FROM AMYOTROPHIC LATERAL SCLEROSIS (ALS) OR CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY (CIDP)

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Background. The Hepatitis E Virus (HEV) is an emerging pathogen and is the main cause of acute jaundiced hepatitis and acute liver failure in developing countries. Neurological manifestations represent the most documented extra-hepatic manifestations. The most commonly described neuropathies are Guillain-Barré syndrome in the variant of Acute Demyelinating Inflammatory Polyneuropathy (AIDP), neuralgic amyotrophy and meningoencephalitis.

Methods. This study aims to evaluate the prevalence of Hepatitis E Virus (HEV) infection, by measuring serum IgG, IgM and HEV RNA and by evaluating HEV RNA in stool, in patients with Amyotrophic Lateral Sclerosis (ALS), healthy controls with the same epidemiological exposure (consisting of caregivers who take care of ALS patients), compared to patients with a chronic inflammatory demyelinating polyneuropathy (Chronic Inflammatory Demyelinating Polyneuropathy, CIDP), and to blood donors representing the general population living in the same geographical area.

Results. The prevalence of anti-HEV IgG positivity was 18.75%, 20% and 33% respectively in subjects with ALS, caregivers and CIDP, resulting significantly higher than that observed in the control group consisting of blood donors paired by age and gender (8.97%). In all the cases examined, there was only evidence of previous HEV infection, since none of the patients examined tested positive for HEV-RNA.

Conclusions. The prevalence of anti-HEV IgG in ALS patients was not different from the prevalence observed in the caregivers group, in fact both groups showed a significantly higher prevalence than that found in the general population. This result allows us to hypothesize that people with ALS and their caregivers have lifestyle (contact with animals) or food habits that expose them to a greater risk of contracting an HEV infection and that genetic factors could determine the probability of develop such neurological pathology following HEV infection. Our study therefore demonstrates for the first time a possible association between previous exposure to HEV and neurological pathologies such as ALS and CIDP, although a safe cause-effect relationship cannot be established.

COVID-19 CONTROL: LESSONS FROM THE “PALAZZO PECILE” OUTBREAK IN ROME

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Background. During 2020, Italy has been one of the most affected Countries by the SARS-CoV-2 epidemics in Europe, with 240.436 confirmed cases and 34.744 deaths reported by June 30th. Further to a first emergency phase relying mainly on social distancing measures (“Country lockdown”), a strategy based on timely testing, contact tracing and isolation has been promoted by the Ministry of Health to control the epidemics. We hereby provide a description of the implementation of this strategy to control a SARS-CoV-2 outbreak in a closed community in Rome (a “squat building” located in Piazza Pecile).

Methods. Following the reporting of five cases of SARS-CoV-2 infection in a family living in a “squat” building in Rome, a strategy based on contact tracing, testing of all inhabitants and isolation of positive cases and close contacts was put in place, in close collaboration with local authorities and Non-Governmental Organizations (NGOs). An assessment of the capacity to conduct home isolation in the building was conducted, and those people who were not deemed in the condition to safely isolate themselves at home were relocated to a dedicated COVID-19 facility, along with all positive cases. Active surveillance of symptoms was continuously performed during the 18 days isolation period, to allow timely identification of suspected cases and early hospitalization of positive cases.

Results. A total of 107 building occupants were tested for infection through a nasopharyngeal swab. Twenty-five people tested positive (with an overall attack rate of 23.4%) and were isolated in dedicated facilities. Tracing of contacts outside the building lead to testing 41 additional people, three of which positive for SARS-CoV-2. All but one case developed within family clusters, with a total of six affected families, including nine positive children aged less than 18 (36%). Only seven people developed symptoms of infection, with asymptomatic carriers accounting for 72% of cases. Infections seem to have been driven mainly by symptomatic patients. Fifty-three people were isolated in dedicated facilities, including prior or after hospitalization, while 46 people completed the whole isolation period inside the building. As a result of all measures undertaken, no new infections occurred within the building during the 18 days isolation period.

Conclusion. A control strategy combining timely case identification, contact tracing, isolation based on an assessment of the specific setting, active surveillance of symptoms, based on a strong cross-sectional collaboration with local authorities, NGOs and different sectors of the Local Health Unit ASL Roma 2, lead to an effective control of the SARS-CoV-2 outbreak in a closed cluster within a 18 days’ timeframe.

IDENTIFICATION OF HUMAN CYTOCHROME P450 ISOFORMS IN PHOSMET BIOACTIVATION AND METABOLIC INTERACTIONS WITH CHLORPYRIFOS

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Background. Organophosphate Pesticides (OPTs) are a class of compounds used in agriculture and on animal for pest control. Human exposure to OPTs is associated to occupational activities or due by residual on food and in water for the general population. Their oxidative desulfuration catalyzed by cytochrome P450 (CYP), causes the formation of a neurotoxic metabolite, called oxon, known to inhibit Acetylcholinesterase (AChE). The potential correlation between exposure to OPTs and neurodegenerative diseases and/or neurodevelopmental effects has been extensively debated in the last years. In this work we studies the human metabolism of Phosmet (Pho) an OPT for which data are not available in a concentrations range of 0.5-300 μ M, representative on human exposure. Moreover, since human may be co-exposed to different OPTs, possible metabolic interactions between Pho and Chlorpyrifos (CPF) was also investigated.

Methods. Pho metabolism was studied using an integrated *in vitro* approach with single human recombinant CYP isoforms, Human Liver Microsomes (HLM) and Human Intestine Microsomes (HIM), determining the kinetic parameters (V_{max} , K_m and C_{li}) and the activity of chemical inhibitors specific CYPs on Phosmet-oxon (PhOx) formation. To analyze and quantify the metabolite formation an *ad hoc* HPLC method was set up.

Results. The characterization of the reaction in single human recombinant CYPs evidenced the main involvement of CYP2C family with a C_{li} ranking of 2C18>2C19>2B6>2C9>1A1>1A2>2D6>3A4>2A6. The major involvement of CYP2C was confirmed by using specific chemical inhibitors in HLM where a single typical kinetic curve, while in HIM a biphasic reaction was evidenced, due to the presence in the gut of the two CYPs 2C and 3A4. Furthermore, Pho could efficiently inhibit both CPF bioactivation and detoxication, while the opposite is not relevant at the actual exposure levels.

Conclusions. Considering the average human hepatic CYP content, CYP2C19 contributed for the great majority (60%) at relevant (low) exposure concentrations, while CYP2C9 (33%) and CYP3A4 (31%) were relevant at high substrate concentration. Accounting for $\frac{1}{4}$ of that measured in the liver, the role of the gut pre-systemic bioactivation was also relevant. The prominent role of CYP2C in oxon formation was not shared by other OPTs for which CYP1A2 and CYP2B6 were the most active CYPs in forming the corresponding oxon at low exposure concentration. Consequently, the peculiar metabolic interaction between Pho and CPF bioactivation and detoxification depends on the different isoform-specific Pho bioactivation when compared to other OPTs.

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

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Background. Over the last decades, the number of health professionals who participate in Continuing Medical Education (CME) through e-learning environment, has grown rapidly due to its flexibility. The main challenges faced are high rate of dropouts (43%). Since 2004, the Italian National Institute of Health (ISS), provides CME e-learning courses in public health, using PBL methodology. A series of variables characterize the different type of courses: low, medium high interaction, accreditation and enrolment modality. The aim of this study is to identify the characteristic of dropout participants in e-learning courses at ISS, delivered between 2017-2019 triennium. To understand key variables that best predict the dropouts and consequently, hypothesize actions to improve retention. At ISS, dropouts are classified as participants who withdraw before or at any point after starting the course.

Methods. Descriptive and inferential statistics were performed. We first analyzed 21 courses (n=44.630 participants) within the triennium. Afterwards we have chosen a single sample course for retrospective analysis. Based on Park's logistic regression model, we classified variables into two categories: Motivational and Individual background characteristics. We also, developed a matrix based on the 7 steps of PBL, to identify the critical points of participants withdrawal. We ran a logistic regression analysis through Stata 11.2 on gender and region. Ongoing more analysis on age, profession, employment type.

Results. On the triennium we found mean dropout rate of 34% and completion rate of 66%, with a great variability according to the level of interaction, enrolment modality, and accreditation. On the sample course, out of 11198 participants, the retention rate is 6356 (56.8%) and dropout rate of 43.2% (n=4842). According to the matrix, many participants dropped at earlier and later stages of the course: earlier leavers (12.4%), soon after T0 (13.7%) and after post-test (10.4%) respectively.

Conclusions. The results shade a light on key variables may be contributing to dropouts, including critical points at the courses offered by ISS. Relevance seems to be the key factor regarding motivational variables. On the other hand, gender and region seem to play a key role on participants to either withdraw or remain in the course.

MATHEMATICAL MODELLING OF FLYING-MOSQUITOES DISPERSAL: A PDE BASED APPROACH

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Background. The general objective of my PhD project is to develop robust quantitative mathematical methods which could contribute optimizing studies and control procedures of mosquito vector of diseases. The study presented here fits into this general objective and focuses on the estimate of dispersal and mortality of *Aedes albopictus*, an important mosquito vector of several arboviruses (e.g. chikungunya and dengue virus) which in the last decades has become a permanent pest in Mediterranean Europe. The quantification of mosquito dispersal represents a crucial parameter for the assessment of the spatio-temporal spread of mosquitoes and the risk of transmission of mosquito-borne diseases.

Methods. To approach this problem, we have treated mosquito dispersion as a diffusion process, which can be modelled through a Partial Differential Equations (PDE). Our model was calibrated using field data obtained from three Mark-Release Recapture (MRR) experiments of *Aedes albopictus* carried out in Padua (northern Italy) in 2009. Specifically, we started from the known analytical solution of the heat PDE equation - a normal bivariate distribution representing the probability of mosquito position at different time steps - and expanded it by including into the model also mosquito mortality. This mortality was estimated from data collected under semi-field conditions carried out during the MRR experiments, by fitting several theoretical functions, using likelihood ratio test, e.g. exponential, Gompertz, Weibull, logistic and temperature dependent functions. The diffusion coefficient D of the PDE and a correction factor (ζ) for the capture rate of sticky traps used for the experiment were estimated through a Markov Chain Monte Carlo procedure.

Results. The best fit of mortality was obtained using an exponential function. The average daily mortality rate was estimated to be 0.02 and 0.01 in the first and in the second/third MRR experiment, respectively. We also estimated different values for the mosquito dispersion parameter D , that can be interpreted as *meters²/hours* traveled by mosquitoes, in the three different MRR experiments. The mean values obtained for D were 76.79 (95% CI 70.87-89.82), 40.13 (95% CI 37.17-46.19), 26.76 (95% CI 22.32-33.81) for the MRR1, MRR2 and MRR3, respectively; an average value for ζ of 78.35 (95% CI 66.87-92.34) was estimated for the three MRR experiments.

Conclusions. Our results provide a novel approach to the analysis of mortality and dispersal from empirical data, which represent instrumental information for better design of mosquito surveillance programs and prevention strategies.

Session II

Clinical and immunological features of COVID-19

Chairpersons

Sara Buezo Montero, Valentina Perri

IN VITRO STUDY OF THE SYNERGISTIC ACTIVITY OF N-ACETYLCYSTEINE ASSOCIATED WITH B-LACTAM ANTIBIOTICS AGAINST NEW DELHI METALLO-BETA-LACTAMASE PRODUCING *ENTEROBACTERIACEAE*

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Background. Increasing antimicrobial resistance has become one of biggest challenge putting at risk the global public health at the beginning of the third millennium, since there is a paucity of effective antimicrobials for the treatment of infections due to Multi-Drug Resistant (MDR) microorganisms. Among *Enterobacteriales*, the production of carbapenemases, which confer the resistance to the last-resort drug carbapenems, appears to be one of the major responsible for the MDR phenotype. In particular, the production of metallo-beta-lactamases such as New Delhi Metallo-beta-lactamase (NDM) in *Enterobacteriales* is particularly worrying. In fact, only the combination ceftazidime/avibactam plus aztreonam has shown some clinical efficacy. Recently, attention has been paid to the investigation of antibacterial activity of some non-antibiotic compounds, such as N-Acetylcysteine (NAC), against MDR gram-negative bacilli. Therefore, in this study we assessed the antibacterial activity of NAC, alone and in combination with different antibiotics, against NDM-producing *Escherichia coli* and *Klebsiella pneumoniae*.

Methods. A total of 18 strains (17 *E. coli* and 1 *K. pneumoniae*) collected from patients admitted to the Department of Infectious Diseases of Sapienza University of Rome were analyzed. The minimum inhibitory concentrations (MICs) were determined for the following antibiotics Meropenem (MEM), Colistin (COL) and NAC by broth microdilution method. Afterwards, the synergistic activity of the combination NAC+MEM was evaluated by the checkerboard method and the calculation of the FIC-index. Synergism was defined as a FIC-index <0.5.

Results. MICs of MEM ranged from 8 to 128 µg/ml, meaning the strains were fully resistant to carbapenems. MICs of NAC for all the tested strains was 2.5 mg/ml. For COL MICs were <0.01 µg/ml for 17 strains whereas the strain of *K. pneumoniae* showed a MIC of 4 µg/ml. The combination of NAC+MEM was synergistic in all the cases.

Conclusion and perspectives. Although preliminary, these results suggest a potential role of NAC in restoring the antibiotic susceptibility of meropenem in NDM-producing *Enterobacteriales*. Therefore, the clinical usefulness of adding NAC to the commonly used antibiotic combinations should be further investigated. To evaluate the susceptibility of the strains to Fosfomycin (FOS) and Aztreonam (AZT) and to test the synergism between NAC+COL, NAC+FOS, NAC+AZT.

VALIDATION OF HUMAN IGG RESPONSE TO *Aedes* SALIVARY PROTEINS AS A NOVEL MARKERS OF HUMAN EXPOSURE TO *Aedes albopictus*

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Background. The recent outbreaks of dengue, Zika, chikungunya and the rapid worldwide spreading of *Aedes albopictus* highlight the need to improve vector surveillance. Human Antibody (Ab) responses to mosquito salivary proteins is emerging as a reliable biomarker for evaluating vector- human contact and the efficacy of control programs. In a previous study we showed that the 34k2 *Ae. albopictus* salivary protein (al34k2) evokes specific IgG response in mice experimentally exposed to bites of tiger mosquito. The present study aims to evaluate the suitability of using specific antibody response to al34k2 as a biomarker for vector exposure in individuals naturally exposed to *Ae. albopictus*.

Methods. ELISA tests were used to measure IgG response to al34k2 and to *Ae. albopictus* salivary gland proteins extracts (alSGE) in sera collected from healthy human blood donors in two areas with different densities of *Ae. albopictus*, Padova (PD, high density) and Belluno (BL, low-moderate density) during two different periods: just before the appearance of *Ae. albopictus* (May) and after the summer period of exposure to mosquito bites (Sept-Nov).

Results and conclusions. IgG responses to alSGE showed a significant increase from low to high mosquito density period in both areas. Moreover, IgG antibody levels were higher in PD than BL during both the low and the high-density mosquito seasons. The anti-al34k2 IgG responses were higher in PD than in BL both in the low-density and shortly after the high-density mosquito season. Contrarily, comparison of IgG antibody levels against al34k2 between the two set of sera collected in Belluno did not show a significant seasonal variation. However, a statistical significance was only reached in Belluno when the analysis was restricted to the paired samples. These results suggest that al34k2 may be a novel reliable candidate as marker to evaluate spatial and/or temporal variation of human exposure to *Ae. albopictus*. This represents a serological tool that combined with entomological and epidemiological methods could enhance surveillance of *Ae. albopictus* spread and the risk of arbovirus transmission and could be used as a direct tool for the evaluation of anti-vectorial measures.

GENOTYPIC AND PHENOTYPIC CHARACTERIZATION OF STAPHYLOCOCCI FROM ATOPIC DERMATITIS PATIENTS

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Background. Atopic Dermatitis (AD) is a chronic, inflammatory and immune-mediated skin disease. AD patients are characterized by a marked skin bacterial dysbiosis, associated with high susceptibility to *Staphylococcus aureus* colonization. This bacterium has a pivotal role in AD pathogenesis and colonizes the skin via biofilm, making its eradication through conventional therapies very hard. However, certain strains of Coagulase-Negative Staphylococci (CoNS) compete with *S. aureus* by a bacteriostatic/bactericide activity or by biofilm disaggregation/inhibition. The purpose of this research is to identify CoNS strains able to control/inhibit cutaneous colonization from *S. aureus* in AD patients.

Methods. *S. aureus* and CoNS isolates, derived from AD patients (sampled at flare (t0) and post flare (t1) phases) and healthy controls, were identified by MALDI-TOF and genotyped by RAPD-PCR. The Antimicrobial Susceptibility Test (AST) was determined using Vitek-2. Biofilm production and biofilm inhibition activity of CoNS were determined through crystal violet staining. The effect of CoNS culture supernatants on *S. aureus* biofilm production was evaluated spectrophotometrically.

Results. *S. aureus* was isolated from skin samples of all AD patients, (with a higher degree of colonization during flare disease respect to post-flare), and of only 25% of healthy individuals. In contrast, the skin of controls and patients sampled at t1 was predominantly colonized by CoNS, with high rates compared to patients at t0. Furthermore, at t0 the nares and the lesional skin of each AD patient were colonized with a single clone of *S. aureus*, which resulted genotypically different from that recovered at t1. Generally, *S. aureus* strains from AD patients at t0 showed a broad spectrum of sensitivity to different antibiotics. However, the strains isolated at t1 exhibited greater resistance. All *S. aureus* strains isolated during both phases were strong or moderate biofilm producers, while those from healthy controls were weak or no biofilm producers. Indeed, CoNS strains from AD patients and controls were weak and no biofilm producers and, interestingly, most of them inhibit the biofilm formation.

Conclusions. *S. aureus* is the main pathogen involved in AD and the inflammatory status could allow the prevalence of *S. aureus* biofilm over the other cutaneous commensals. Thus, the modification of skin biofilm community, through the topical application of CoNS with probiotic activity, could represent an interesting therapeutic strategy for *S. aureus* eradication.

PERSONALISED EXERCISE TRAINING PROGRAMME FOR HIV-INFECTED PATIENTS: EFFECTS ON EXERCISE TOLERANCE AND IMMUNE ACTIVATION

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Background. With the widespread use of Antiretroviral Therapy (ART) in high income settings, cardiovascular disease emerged as an important cause of death in patients with HIV due to the decreasing incidence of opportunistic diseases. Chronic inflammation facilitates the development of accelerated atherosclerosis and myocardial dysfunction, with a possible contribution from both HIV and ART. Physical activity is being increasingly recommended to reduce cardiovascular risk among HIV-infected patients. Finding of reduced exercise tolerance at Cardiopulmonary Exercise Testing (CPET) strongly relates with an increased risk of death in several cardiac and pulmonary diseases. However, the relationships between physical activity and exercise tolerance as well as immune activation have not been systematically investigated among HIV-positive patients yet.

Methods. Thirty-five patients on ART due to known infection from HIV-1 were longitudinally recruited and allocated into training (N=19) and control (N=16) groups. Each participant underwent the same investigations at baseline (t_0) and 12 weeks later (t_1): CD4⁺, CD8⁺, CD3⁺ and CD8⁺/CD38⁺ T-cells count; blood HIV-1 RNA testing and tailored incremental and constant-work rate CPET. The training programme consisted in a total of 36 one-hour sessions to be performed unsupervised over 12 weeks. Every patient in the training group was provided with detailed instructions from an illustrated manual and a pulse watch. Exercise intensity (i.e. low, moderate and high) was individually defined according to the heart rate response observed during CPET at t_0 .

Results. All participants had undetectable HIV-1 RNA. Comparable T-cells count was found between the two groups at t_0 . Poor compliance with the training programme was registered in the training group, with an average of 17.8 ± 10.0 sessions performed. No improvement in peak oxygen uptake at CPET was found in both groups. However, lactate threshold (15.7 ± 3.9 vs 17.0 ± 3.8 ml/kg/min, $p=0.033$), peak oxygen pulse (13.8 ± 2.6 vs 14.1 ± 3.0 ml/beat, $p=0.047$), as well as endurance time (448.2 ± 205 vs 695.4 ± 449.2 sec, $p=0.003$) significantly improved with training. Furthermore, CD8⁺/CD38⁺ cells count significantly decreased in training group compared with controls (-4.3 ± 3.1 vs -0.3 ± 0.5 cells/ μ l, $p<0.001$). Significant correlations were observed between the number of training sessions and the change in CD8⁺/CD38⁺ cells count ($r=-0.575$, $p=0.013$) and endurance time ($r=0.738$, $p<0.001$).

Conclusion. Twelve weeks of unsupervised, personalised physical training seem to positively affect physiological response to exercise and immune activation among HIV-infected patients. Nevertheless, poor compliance is common and might represent an important limitation to the expected benefits of physical activity.

IMPACT OF CHLAMYDIA TRACHOMATIS ON HUMAN SERTOLI CELLS IN THE ETIOPATHOGENESIS OF MALE INFERTILITY

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Chlamydia trachomatis has recently acquired clinical importance in male infertility for it is known to disseminate to the upper genital tract, causing epididymitis or epididymo-orchitis, well established risk factors for infertility, although, to date, the correlation between *C. trachomatis* and male infertility is still largely unexplored. In recent years, it has been hypothesized that *C. trachomatis* might contribute to male infertility by altering the testicular epithelium via the infection of Sertoli cells. Sertoli cells are key elements for the spermatogenesis, guiding germ cell development and protecting them against infectious agents through the activation of innate immune pathways like toll-like receptors. Herein, we investigated, for the first time, the cellular and molecular mechanisms underlying *C. trachomatis* infection of primary human Sertoli cells in the etiopathogenesis of male infertility. To do so, we set up an *in vitro* infection model of primary human Sertoli cells with *C. trachomatis* serovar D to study the integrity of F-actin, Vimentin and Tubulin fibres by confocal microscopy, and the host cell response to *C. trachomatis* via the determination of TLRs as well as the respective signaling pathways and inflammatory cytokines (e.g. IL-1 α , IL-6 and IFNs). Our results demonstrated *C. trachomatis* ability to infect Sertoli cells as well as to remain within them for a long time, inducing a generalized alteration of the cell cytoskeleton. In particular, this was characterized by the lack of F-actin ring surrounding chlamydial inclusions, that might explain the absence of cell lysis observed in *Chlamydia*-infected Sertoli cells up to 96 hours post infection. Lastly, the prevalent activation of TLR3 followed by the inhibition of NF- κ B and IRF-3 and the absent production of inflammatory cytokines, as demonstrated in our study, hinted to the hypothesis that *C. trachomatis* might evade the host-cell response, and, hence, generate a chronic infection. Overall, our data suggest possible mechanisms underlying the disorders of the male reproductive system caused by *C. trachomatis* infection.

IMPACT OF ANTIRETROVIRAL THERAPY ON GUT CD4 T CELLS ACTIVATION: DIFFERENCES BETWEEN NAÏVE AND LONG-TERM TREATED HIV-1 INFECTED PATIENTS

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Background. A rapid and substantial damage of the gastrointestinal tract occurs during Human Immunodeficiency Virus-1 (HIV-1) infection, with a massive depletion of T helper type 17 (Th17), a CD4+ T cell subset involved in normal mucosal defense and epithelial barrier maintenance. This loss is linked to chronic levels of immune activation, that persist despite Antiretroviral Therapy (cART).

Methods. Twentytwo male HIV-1-infected individuals, eleven undergoing long-term fully suppressive cART (>5 years) (group A) and eleven HIV-1 cART naïve patients (group B) were enrolled in this study. Lamina Propria Lymphocytes (LPL) were freshly isolated from gut biopsies collected by pancolonoscopy. The expression of immuno-activation markers CD38 and HLADR and IFN-gamma or IL-17A in CD4+ T-Cell, Th1 and Th17 respectively, was evaluated by multiparametric flow cytometry analysis and expressed by median frequencies. Comparisons among patient groups were performed using the Mann-Whitney test. The level of significance was set at 0.05.

Results. The cART-naïve HIV+ patients (median age: 46; IQR 39-49) had a detectable plasma viral load >50 copies/ml, with a CD4+ T cell count ranged from 277 to 621 cells/mm³, while ART-treated HIV+ individuals (median age: 48; IQR 32-56) were virologically suppressed and showed a peripheral blood CD4+ T cell count ranged from 708 to 1350 cells/mm³. A statistically significant reconstitution of intestinal CD4+ T cells percentage was observed in Group A (median 11%; IQR 7.5–16.1) as compared to Group B (median 46.12%; IQR 42.4–51.2) ($p < 0.0001$). Regarding the effects of antiretroviral treatment on immune activation levels, our findings indicated that the frequencies of CD4+ T cells expressing CD38+ and/or HLA-DR+ decreased in Group A compared to Group B [CD4+ CD38+: 6.5% versus 40% ($p = 0.005$); CD4+ HLA-DR+: 5.8% vs 17.8% ($p = 0.001$); CD4+ CD38+ DR+: 9.2% versus 1.3% ($p = 0.004$)] Interestingly, data, obtained from a comparison of Th1 and Th17 T cells frequencies between cART-treated and naïve patients, highlighted no significant differences between the two groups.

Conclusion. Although long-term antiretroviral therapy resulted in a significant increase in the levels of total CD4+ T-cells in gut mucosa and in decline of T-cell activation, it fails to restore the frequencies of Th1 and Th17. To this extent, cART may not be effective on the complete recovery of the gastrointestinal damage during HIV-1 infection.

GLIA-NEURON CROSSTALK DURING-HSV-1 INFECTION

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Background. Herpes Simplex Virus type 1 (HSV-1) causes a contagious infection that affects approximately 60% to 95% of adults worldwide, associates mainly with infections of the mouth, pharynx, face, eye, and 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. 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. Despite the fact that we already know something about the role of glia during HSV-1 infection of the brain, it is still unknown whether glial activation is protective or harmful or, more likely, whether this depends on the stage of the disease. The aim of the study is to investigate the glia-neuron crosstalk during HSV-1 infection and its role in neuronal damage.

Methods. Primary cultures were obtained from rat and mice embryo brains according to the standard protocol. To obtain pure neurons Cytosine arabinoside was added to inhibit the growth of glia. Confluent cellular monolayers were infected with HSV-1 and analyzed by Western Blot and confocal microscope. HSV-1 titers were measured in conditioned media by standard plaque assay.

Results. In order to investigate the glia-neuron crosstalk during HSV-1 infection, mixed co-cultures were infected with HSV-1 and after 24h the conditioned media (sup) was treated with UV to inactivate the neo-formed virions and transferred onto neurons or mixed co-cultures (pretreatment) for 24 h. Then, the cellular monolayers were infected with HSV-1. After 20h, the viral titer was quantified by standard plaque assay: HSV-1 infection resulted to be inhibited in pretreated co-cultures (about 1.5/2 log) respect to unpretreated one. These data suggested that sup from HSV-1-infected Mixed co-cultures contains some cytokines, as well as Interferon type 1 (INF-I), know to induce an antiviral program, and/or IL-6, know to trigger inflammatory genes (including INF-I) transcription via Nf-kB or STAT3. Then, the subcellular distribution of p65 was studied. We observed that during HSV-1 infection (with or without pretreatment) p65 moves from cytoplasm to nucleus, and there its phosphorylation state was significantly increased in pretreated samples respect to mock-infected and unpretreated HSV-1-infected cells. The involvement of HSV-1 infection in the induction of a neuroinflammation condition suggests the use of antiviral molecules with anti-inflammatory activity. Set of potential molecules were screened; the most active molecule (GT 2.9) was tested on HSV-1-infected Vero cells and mixed co-cultures and it was able to inhibit viral replication when was added after the adsorption phase of the virus life cycle. The analysis of the GT 2.9-induced inhibition mechanism revealed a reduced activation of two transcription factors, involved in several pathways including inflammatory ones: Nf-kB and Nrf2.

EVOLUTION OF FIBROSIS INDEXES, LIVER FUNCTION AND CARBOHYDRATE AND LIPID METABOLISM IN PATIENTS WITH CHRONIC HEPATITIS C WHO HAVE ERADICATED THE INFECTION

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The research project was carried out within the scientific activities carried out by INMI Lazzaro Spallanzani in the field of control and treatment of Chronic Hepatitis C virus infection (chronic hepatitis C; CHC). CHC is a chronic infection associated with significant morbidity and mortality at global level. This infection causes a significant number of clinical manifestations resulting from liver damage and altered glycid and lipid metabolism. As of 2015 INMI Lazzaro Spallanzani has coordinated the network for access to new therapies against CHC with drugs with Direct Antiviral Action (DAA). Although these new drugs have proved capable of treating the infection in almost all treated subjects, it is not yet clear what is the clinical impact on patients' health in the medium and long term.

The work program was created to answer this question and involves some of the main centers of the Lazio Region network for the access to therapy with DAA. The program included the design and the implementation of 3 observational cohorts.

Cohort 1 assessed the impact of AED therapy on the improvement of liver disease in patients who had access to DAA, and resolved CHC, with liver cirrhosis already present. This cohort studied 360 subjects with an average follow-up of 2 years. The analysis showed that the incidence of liver cancer is not significantly lower than expected. However, liver compensation indices remained stable and mortality was significantly lower than expected.

Cohort 2 assessed the time course of non-invasive liver fibrosis evolution indexes in patients who had access to treatment, and resolved CHC, with advanced liver fibrosis. A total of 98 patients with an average follow-up of 1 year were analyzed. The results showed a significant improvement of all liver fibrosis indexes analyzed (acoustic impedance, APRI and FIB-4).

Cohort 3 evaluated the temporal trend of compensation indexes of lipid and glycid metabolism in patients who had access to treatment, and resolved CHC, prior to the development of liver cirrhosis. A total of 94 patients with an average follow-up of one year were analyzed. The results do not suggest a significant improvement in glycidic metabolism indices (HOMA stable score). With regard to lipemia indices, an increase in total cholesterolemia was observed, essentially due to the LDL cholesterol fraction.

These analyses suggest that the resolution of CHC is associated with an improvement in the liver disease while the impact on metabolic compensation remains controversial.

PSYCOSEXUAL HEALTH AND SYSTEMIC, MUCOSAL IMMUNE ACTIVATION IN HIV-INFECTED ART SUPPRESSED AND UNINFECTED WOMEN: EVALUATION OF BIOMARKERS AND ENVIRONMENTAL STIMULI

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Background. Despite successful ART, HIV infection in women remains a grave concern over the years in disproportionate ratios as compared to men. It is directly proportional to various reproductive and hormonal differences making women more vulnerable. Immune response elicited can be monitored by analysing various biomarkers in the plasma, serum and vaginal lavage, mucosal immunity, sexual behaviour and other vaginal infections.

Methods. We enrolled 53 subjects, 23 HIV Positive women on successful HAART and 30 Healthy Women (HW) without statistical differences in age. Cytometry and Kit ELISA (R&D) were used for estimation of lymphocytes and all cytokines. Subjects were also tested for co-morbidities like diabetes, HCV, cervical cancer etc. Statistical analysis was performed using PRISM 8.0.

Results. Both groups had similar CD4. HW women had a higher CD4/CD8 ratio and CD8 cell count as compared to infected (respectively $p=0.004$, $p=0.007$). Plasma levels of sCD163, CXCL-10, IL-1, IL-6 and IL-8 were significantly higher in HIV women than HW ($p<0.001$), while IL-6 and IL8 were lower in the VL of HIV women. Regarding PAP test, only an ASCUS in HW was found. Moreover, estradiol levels correlated to plasmatic CXCL-10 ($r=-0.7$, $p=0.005$) and vaginal CXCL-10 ($p=0.02$, $r=-0.57$). HIV positivity and sexual dysfunction ($p=0.03$) are correlated. A significant difference between the two groups in the FSFI score ($p=0.02$) was found, particularly in sexual desire and lubrication (50% HIV, 26% HW). A positive correlation between level of testosterone and FSFI score was found in HIV women only ($p=0.005$; $r=0.56$). Testosterone and age too were correlated ($p=0.008$, $r=-0.52$). The HIV group depicted a correlation between testosterone and plasmatic sCD14 ($p=0.03$, $r=0.53$), CXCL-10 ($p=0.04$, $r=-0.52$), IL-6 ($p=0.01$; $r=-0.51$). Both groups had similar anxiety disorder: 27% in HIV positive and 25% in HW. Z-index was associated with orgasm domains ($p=0.01$; $r=-0.4$) and CD4+ T cells ($p=0.02$; $r=-0.45$).

Conclusion. A dissociation between plasma and mucosal immune activation is observed with high plasma levels and decreased levels in mucosal environment in HIV positive women under successful HAART. Female sexual dysfunction seems to be associated with HIV positivity and testosterone levels. The underlying gap in the quality of life of young healthy and HIV women needs to be bridged.

STUDYING OF EXTRACELLULAR PROTEINS OF ASPERGILLUS

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Background. A growing mold problem invasive, chronic and allergic mold infections caused by *Aspergillus* are a major source of morbidity and mortality in both immunosuppressed and immunocompetent hosts. The overall annual incidence for acute invasive aspergillosis among the immunosuppressed patient population varies from approximately 2 to 10%. Exoproteins are the primary fungal components involved in host–fungal interactions. The exoproteins of *Aspergillus* such as ribotoxin, thioredoxin reductase, mitogillin are important factor of virulence. Also nowadays therapeutic options for aspergillosis are limited. Overcoming this growing threat requires a better understanding of therapeutic strategies to mitigate resistance, new drugs with novel mechanisms of action, and a commitment to new molecular technology that can rapidly identify *Aspergillus* with a simultaneous evaluation of drug resistance. Study the extracellular proteins of *Aspergillus fumigatus* characterizing them and studying the pathway that regulates their production and secretion in order to find both new agents to fight *Aspergillus* infections and a new fast diagnostic method (MALDI-TOF) to identify the infection in the sputum.

Expected (or preliminary) Results. It was performed characterization and evaluation of the quantity of production of exoproteins from different reference strain of *Aspergillus spp.* growth in different cultural conditions. We have collected 452 sputum sample and 6 samples of bronchoalveolar lavage, from a patient with cystic fibrosis, coming from UOC Microbiology and Virology directed by professor Antonelli. It was compare the results of electrophoresis of sputum, bronchoalveolar lavage fluid and *Aspergillus*'s cultural fluid. It was found that 18 kda protein (mitogillin) present only in infected by aspergillus sputum. We also have evaluated activity of selective epigenetic inhibitor compounds synthetized in the laboratory directed by professor Antonello Mai (Department of Drug Chemistry and Technologies) on expression of virulence-related exoproteins produced by *Aspergillus* species. The results of activity of selective epigenetic inhibitor compounds have showed that bromodomain extra terminal protein inhibitor and pan-histone demethylase inhibitor significantly decreased the level of extracellular proteins and reduced mycelial growth.

Future perspectives. It will be demonstrated the usefulness of the new extracellular proteins database in MALDI-TOF MS by the use of procedure for the identification of proteins from *Aspergillus spp.* from sputum, bronchoalveolar lavage. It will be studied the mechanism of action of selective epigenetic inhibitor compounds on production of extracellular proteins.

UREAPLASMA SPP INFECTION IN SOLID ORGAN TRANSPLANT: PROSPECTIVE CLINICAL STUDY

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Background. Increasing evidence suggests that disseminated *Ureaplasma* infection cause the hyperammonemic post-transplant idiopathic syndrome in lung transplant recipient. Objective of our study is to evaluate the prevalence of *Ureaplasma* spp infection in solid organ transplant recipients who receive the transplant at Policlinico Umberto I Hospital and to monitor the incidence of the syndrome in our population.

Methods. At the Transplant Unit of Policlinico Umberto I Hospital in Rome, patients who underwent kidney, liver and lung transplantation were enrolled. Specimens were obtained after the transplant. Urine samples were collected from each patients. Broncho Alveolar Lavage (BAL) and bile were collected from liver and lung transplant patients, respectively. Conventional PCR was used to identify a specific DNA fragment of *Ureaplasma Urealyticum* (UU). The bacterial DNA was extracted from samples using the QIAamp DNA Mini Kit (Qiagen, Germany) according to the manufacturer's protocol. Bacterial DNA amplification was performed in a GeneAmp® PCR system 9700 Thermal Cycler (Applied Biosystems, US). The PCR assay was conducted using specific primer (UMS170/UMS263) for the multiple-banded antigen gene of UU (476bp). Positive and negative control were also included. The positive control used in this study was the extracted DNA of clinical specimen-positive to UU. After PCR run, amplified material was analyzed by electrophoresis in 1.5% agarose gel (Promega, USA) and specific product was visualized on UV transilluminator. The amplicon sizes of 476bp detected by PCR was considered positive for UU.

Results. Twenty-eight patients (7 females, 21 males) were enrolled. Overall, of the 28 patients who underwent transplantation, the 39.3 % (11/28) received a kidney transplant, the 32.1% (9/28) lung and the 28.6 % (8/28) a liver transplant. The 14% (4/28) of patients had died following complication after the transplantation. Conventional PCR was used to identify a specific 476bp fragment of UU DNA in clinical specimens of transplanted patients. A preliminary evaluation was performed on urine of 14 patients (43% lung, 28.5% kidney, 28.5% liver transplant). PCR results showed that 21.4% (3/14) of samples were positive to UU DNA. The patients who showed positivity to UU on urine samples were also screened for BAL. PCR was negative on BAL samples.

Conclusions. According to our preliminary results, *Ureaplasma* spp infection is highly prevalent in our cohort but more data are needed to evaluate risk factors associated with post-transplant dissemination.

INFECTIOUS RISK IN OCRELIZUMAB-TREATED MULTIPLE SCLEROSIS PATIENTS

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Background. Anti-CD20 monoclonal Antibodies (mAbs) have revolutionized the treatment of Multiple Sclerosis (MS), however are associated to an increasing infectious risk. Cytomegalovirus (CMV) is a herpesvirus, which has the potential to reactivate from latency; its reactivation has been described in immunocompromised patients treated with anti-CD20 rituximab. Recently, a new anti-CD20 mAbs named Ocrelizumab (OCR) was licensed for MS. Due to the homology with rituximab, OCR-treated MS patients should be monitored for reduce CMV complications. The first part of this project is to evaluate the presence of CMV through molecular analysis in a cohort of OCR-treated MS patients. Moreover, given that CMV has been implicated in MS protection due to the reconfiguration of the Natural Killer (NK) subset, the secondary aim is to characterize NK-cell in order to investigate correlation between NK and MS clinical outcome and identify an early biomarker of CMV reactivation.

Methods. At the Neuroinfectious Unit of Policlinico Umberto I, MS patients were enrolled. For each patient, a venous blood sample was collected before the start of OCR (T0) and after 6 months (T6). Plasma and Peripheral Blood Mononuclear Cells (PBMC) were obtained according to the manufacturer's instruction. Viral DNA was isolated from 200 μ l of plasma and 1×10^6 PBMC using High Pure Viral Nucleic Acid Kit (Roche, Germany). SYBR Green real-time PCR assay was performed on LightCycler 2.0 (Roche Diagnostics).

Results. 11 OCR-treated MS patients were enrolled (6/5 male/female) with a median age of 49 (IQR: 46-54.5). At T0, the median EDSS (Extended Disability Status Scale) score was 4.5 (IQR: 1.87-5.5) and median age of disease was 12 years (IQR: 7-18). At T0, serological analysis showed that 9/11 (82%) patients were CMV IgG+. No evidence of recent CMV infection (IgM+) were identified. Real-Time PCR was used to detect CMV DNA in PBMC and plasma of 11 OCR-treated MS patients monitored at T0 and T6. Among CMV IgG+ patients 6/9 were positive for CMV DNA; IgG- patients were negative for CMV DNA. Overall, we analyzed 22 plasma and 22 PBMC samples. At T0, CMV DNA was detected in 5/11 PBMC. At T6, CMV DNA was detected in 3/11 PBMC and in 2/11 plasma samples.

Conclusions. These preliminary results showed that in our cohort, CMV DNA was found at higher frequencies in PBMC (18%) than in plasma (4.5%). Likely, because PBMC are a major site of latency of CMV. Moreover, PCR results showed that two patients were positive for CMV DNA in plasma, 6 months after starting OCR. This might suggest a subclinical reactivation due to the release of the virus from the infected cells. In immunocompromised MS patients, CMV reactivation may cause severe organ-diseases. In order to minimize potential CMV infectious risk, MS patients should to be monitored during OCR treatment. To date, we are expanding the cohort by enrolling new OCR-treated MS patients and we are continuing the follow-up until 12 months, in order to perform further cytofluorimetric analysis.

LIMITED IMPACT OF LONG LASTING INSECTICIDE TREATED NETS (LLINs) ON MALARIA TRANSMISSION IN A RURAL VILLAGE OF BURKINA FASO: THE ROLE OF MOSQUITO BEHAVIORAL PLASTICITY

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Background. Long Lasting Insecticide treated bednets (LLINs) are the main malaria vector control strategy, with 3-year mass distribution campaigns recommended by WHO. Nevertheless, reduced LLINs efficacy is occurring in some Sub-Saharan countries (e.g. Burkina Faso) where the annual malaria incidence remains still high. Among many causal factors accounting for this scenario, a crucial role is played by insecticide resistance and changing in mosquito biting behavior, parameters that the PhD project attempts to investigate. Thanks to entomological surveys conducted in Goden village (Burkina Faso) a year after LLINs introduction (occurred in 2010) and during subsequent mass distribution campaigns, we observed: i) decrease of mosquito human-feeding in favor of animals; ii) altered biting time diverted from the typical mid-night peak. These evidences might explain the high mosquito infectivity rates (5.8%-6.6%) constantly observed through ten years in Goden despite LLINs usage. We here further investigate mosquito behavioral changes in response of LLINs, comparing data from recent samplings with those conducted previously in the village.

Methods. During 2019 rainy season, indoor-outdoor collections of host-seeking mosquitoes were performed by: i) BG-traps with BG-lure and fermenting yeast, while a man was sleeping under LLIN indoors; ii) Human Landing Catches (HLC) in absence of LLIN. The sampling protocols followed the same condition of BG trapping and HLC collections conducted, respectively, in 2011 and 2015.

Results. In 2019, *Anopheles gambiae* s.l. mosquitoes were collected more outdoors than indoors by BG-traps (31% IN vs 69% OUT; $t=-5.85$; $p<0.005$; $N=902$), conversely 65% of mosquitoes were collected by BG-traps indoors in 2011 ($t=9.18$; $p<0.0001$; $N=418$). HLC in 2019, collected *A. gambiae* s.l. without differences between indoors and outdoors ($U=729$; $p=0.31$; $N=2,616$), confirming results obtained in 2015 ($U=0.52$; $p=0.74$; $N=1,944$).

Conclusions. The increased vector outdoor biting observed in 2019 is mainly driven by diversion-effect exerted by LLINs. A strong exophagy is not visible in local vector population if humans are readily accessible, as observed for HLC collections in 2019 and 2015, suggesting an opportunistic biting behavior not genetically selected by the continued presence of LLINs in Goden. The high endophagy reported in 2011 might be due to a limited repellent effect of LLIN brand used at that time in the village. Overall our results highlight an inner behavioral plasticity of vector population, which can promptly react to bednets pressure adopting reversible changes in biting behavior. Such plasticity could be causative of LLIN limited impact in Goden and should be accounted for future malaria control strategies.

FIRST DRAFT OF A MIRNA CATALOGUE FROM *ANISAKIS PEGREFFII* INFECTIVE THIRD-STAGE LARVAE AND EXOSOMES-ENRICHED FRACTION

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Background. Anisakiasis is an emerging fish-borne zoonotic disease caused by third-stage (L3) nematodes of the genus *Anisakis*. The disease is characterized by gastrointestinal, ectopic or allergic reactions, following the ingestion of infected raw or undercooked fish or squids. Like other nematodes, they cause even chronic infections and mechanisms of host-manipulation are still unknown. Secreted parasitic molecules, such as proteins, extracellular vesicles and miRNAs, have been proposed to play a relevant role in host-parasite interactions. The aim of the study was to characterize miRNAs of *Anisakis pegreffii* infective L3 and their released exosomes.

Methods. Three biological samples of pools of *A. pegreffii* from *Merluccius merluccius* (FAO37) L3 and of the exosomal-enriched fraction (EVs), obtained from L3 incubation in RPMI for 24h at 37°C, were used to isolate the enriched small-RNA fractions for RNA-seq. Libraries and sequencing were performed on Illumina (Hi-Seq2500) at the EMBL Genomic Core Facility (Heidelberg, DE). After trimming with cutadapt 1.9.1., processed reads were mapped to the available assembly of the *Anisakis simplex* genome (As14 in Wormbase) and then to *A. simplex* ribosomal sequences, using Bowtie. With the aim to obtain a comprehensive *Anisakis* miRNAs catalogue, pooled sequences were used for hairpin and mature miRNAs predictions with miRDeep*. Moreover, hairpin and mature *Ascaris suum* miRNAs were also used to search for orthologues in the *A. simplex* genome. Two selected miRNAs were validated by Stem&Loop PCR.

Results. A mean of 33 million and 24 million raw reads were obtained for the triplicates of L3 and exosomal-enriched fraction, respectively. Filtered reads were 26 and 20 million for L3 and EVs, while, after depletion of ribosomal RNAs, reads mapped to As14 were on average of 12 million for L3 and of 6 million for EVs. miRNA prediction analyses allowed for the identification of 150 (miRDeep*) to 180 (*A. suum* BLAST search) putative novel miRNAs. Comparative analysis provided a first list of 31 highly reliable *Anisakis* miRNAs, two of which (miR1 and miR7) were validated by Stem&Loop PCR.

Conclusions. These preliminary results provide the first draft of the *Anisakis* miRNA catalogue, allowing comparative analyses with other parasitic nematodes. Moreover, identification of potentially targeted genes in human accidental host may shed some light on mechanisms of host manipulation by anisakid nematodes.

LACTOFERRIN AGAINST INFLAMMATORY AND IRON DISORDERS IN DIFFERENT INFECTION MODELS

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Lactoferrin (Lf) is a cationic glycoprotein able to chelate two ferric ions per molecule. Human Lf (hLf), a key element of host defenses, is secreted by exocrine glands and by neutrophils. HLf and bovine Lf (bLf), possessing high sequence homology, exert identical functions, such as antimicrobial and antiviral activities. In the last decades, other important Lf activities have been discovered, including the anti-inflammatory one. This Lf's function is strictly dependent by the binding with specific host cell receptors, leading to Lf cell internalization and translocation into the nucleus, thus directly down-regulating pro-inflammatory genes' expression. In this regard, our group has recently demonstrated the bLf ability in counteracting the tight interplay between inflammatory and iron homeostasis disorders in inflamed macrophages, by down-regulating Interleukin (IL)-6 synthesis and rebalancing the expression of main iron-handling proteins, namely Ferroportin (Fpn), Transferrin Receptor 1 (TfR1) and Ferritin (Ftn).

Here, the role of bLf in different infection models is presented, highlighting its ability to exert a potent action against infection as well as iron and inflammatory disorders.

The first model regards a Cystic Fibrosis (CF) mice suffering from *Pseudomonas aeruginosa* chronic lung infection. Treatments with aerosolized bLf for 7 days were effective in significantly reducing pulmonary bacterial load. Furthermore, for the first time, we showed that bLf treatment was effective in rebalancing the expression of both iron exporter Fpn and iron storage Ftn, thus reducing pulmonary iron overload.

The second model concerns the role of bLf against *Chlamydia trachomatis* infection *in vitro* and *in vivo*. *C. trachomatis*, an obligate intracellular pathogen causing infections associated to inflammation, requires iron for its replication. In *in vitro* study bLf interferes with *C. trachomatis* entry into human epithelial cell line when cell monolayers were pre-treated or treated with the protein at the moment of the infection. Lf exerts a potent anti-inflammatory activity down-regulating IL-6 and IL-8 synthesis as well as rebalancing the expression of Fpn and TfR1 in infected cells. In addition, pregnant women asymptotically infected by *C. trachomatis*, after 30 days of bLf intravaginal administration, were negative for *C. trachomatis* with a decrease of cervical IL-6 levels.

The third and last model regards the *in vitro* study of bLf antiviral activity against the new coronavirus infection (SARS-CoV-2). The coronavirus infection causes severe acute respiratory syndrome characterized by massive systemic levels of pro-inflammatory cytokines. In *in vitro* preliminary results, bLf, through its competitive binding with viral component(s) and its interaction with host surface receptors, blocks SARS-CoV-2 entry in different cell models. Moreover, the efficacy of oral and intranasal administration of bLf against SARS-CoV-2 is demonstrating in paucisymptomatic patients without side effects.

GRAM-NEGATIVE SEPTIC THROMBOSIS IN CRITICALLY ILL PATIENTS: A RETROSPECTIVE CASE-CONTROL STUDY

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Background. Data on septic thrombosis caused by Gram-Negative bacilli (GN-ST) in Intensive Care Unit (ICU) patients are currently limited.

Methods. The aim of this retrospective case-control study (matched 1:3) performed over a 15-month period on ICU patients with bacteraemia, associated (cases) or not (controls) with GN-ST, was to assess 30-day mortality and clinical/microbiological features of GN-ST.

Results. During the study period, 16 patients with GN-ST and 48 controls were analyzed. Polytrauma was the cause of ICU admission in 12 (75%) cases and 22 (46%) controls ($p=0.019$). In no case of septic thrombosis was surgical debridement performed. The site of venous thrombosis was more frequently in the lower limbs, associated with bone fracture in nine out of 12 (75%) cases. The median duration of bacteraemia (22 days vs 1 day; $p<0.001$) and time to clinical improvement (15 days vs 4 days; $p<0.001$) were significantly longer in cases than in controls. On analysis of the Receiver Operating Characteristics (ROC) curve, bacteraemia >72 h was significantly associated with GN-ST (Area Under the Curve (AUC) 0.95, sensitivity 0.996 and specificity 0.810; $p<0.001$). Finally, 30-day mortality was 20% in cases and 67% in controls ($p<0.001$).

Conclusions. Critically ill patients with GN-ST showed specific clinical features. Despite delayed bacteraemia clearance, targeted antibiotic therapy plus anticoagulation usually provided clinical improvement and a low 30-day mortality rate.

THE BURDEN OF INFECTIONS IN SEVERELY INJURED TRAUMA PATIENTS ADMITTED TO THE INTENSIVE CARE UNIT

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Background. Infections following severe injury are common and have a major impact on patient outcomes. Developing an infection is associated with increased critical care use, hospital stays and mortality. Infections caused by multidrug resistant microbes (especially Carbapenem Resistant *Klebsiella Pneumoniae*- CRKP) play a major role in morbidity and mortality of trauma patients. The aim of this study was to describe the incidence of infections in severely injured trauma patients. Furthermore, we aimed to identify admission characteristics that are associated with infection and to evaluate outcomes in those patients who developed an infection during critical care admission. Moreover, we collected data about CRKP colonization and infections.

Methods. A prospective cohort study of severely injured adult patients admitted to critical care was conducted. Data were collected prospectively on patient and injury characteristics, baseline physiology. Patients were followed up for infectious episodes and other adverse outcomes while in the hospital, during a 3-years period (from January 2017 to June 2020). The severity of polytrauma was determined with the Injury Severity Score (ISS).

Results. We enrolled 120 patients with an ISS greater than 15. Within the first 48 hours, 15 (12,5%) patients died, leaving a cohort of 105 patients available for analysis. 76% of patients developed at least one infection, and there were 95 infections diagnosed overall. The most prevalent infectious complications affected vascular catheters (26%), and lower respiratory tract (26%), whereas urinary tract infections were diagnosed in 21% of cases and central nervous system infections in 10% of cases. 10% of patients suffered from surgical site infections and 5% from gastrointestinal infections. There were no significant differences in age, sex, mechanism of injury, or injury severity between patients who developed infections and those who did not. Increased severity of shock on admission was the only variable associated with the subsequent development on infection. Moreover, infection rates were greater with shock. Median time to first infection was earlier for all degrees of shock compared with those patients not shocked on admission ($p=0.01$). KPC-producing *K. pneumoniae* was detected in 48 patients (46%). In 75% of cases, the detection of carbapenem-resistant *K. pneumoniae* was associated with an infection.

Conclusions. Infectious complications are a burden for severely injured patients and occur early in the critical care stay. Severity of admission shock was predictive of infection and represents an opportunity for interventions to improve infectious outcomes.

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

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Background. *Neisseria Meningitidis* of serogroup C (MenC) belonging to clonal complex (cc) 11 is 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 MenC cases 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. This study aims to describe the epidemiology and the main characteristics of MenC responsible of IMD in Italy from 2017 to 2019. Moreover, genetic relationships among MenC isolates circulating in the country were also evaluated.

Methods. Bacterial isolates and clinical samples (blood and/or cerebrospinal fluid) from IMD cases are collected and characterized at the National Reference Laboratory (NRL) of Istituto Superiore di Sanità (ISS) in Rome. Antimicrobial susceptibility was determined by MIC Test Strip Methods and interpreted according to the EUCAST breakpoint. Genotypic characteristics, including Multilocus Sequence Typing (MLST), finetype, and antimicrobial resistant genes were performed and analysed using the PubMLST database (<https://pubmlst.org/neisseria/>). Moreover, phylogenetic analysis of a subsample of MenC isolates were performed by core genome MLST (cgMLST).

Results. A total of 142 laboratory confirmed cases due to MenC were reported within the National Surveillance System (<http://old.iss.it/mabi>) from 2017 to 2019. Of them 107 were sent to NRL at ISS. The MenC IMD showed an average annual incidence of 0.07 per 100.000 inhabitants. The median age was 28 years. The main clinical picture was sepsis, followed by meningitis and meningitis/sepsis. The case fatality rate was 25%. Two isolates were resistant to rifampicin (MIC>0.25 mg/L) and 1 isolate was resistant to penicillin (MIC>0.25 mg/L). Moreover, 50% of MenC showed a decreased susceptibility to penicillin G. Six different ccs (cc11 was the predominant), and 11 genotypic formulas- the most frequent C:P1.5-1,10-8:F3-6:ST-11(cc11)- were identified. Phylogenetic analysis based on cgMLST clustered the genomes by ccs. In particular, 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. In Italy, MenC continues to be responsible of severe IMD cases. From 2017 to 2019, C:P1.5-1,10-8:F3-6:ST-11(cc11) is the main strain responsible of outbreaks during the last years. In the post vaccination era, monitoring and genomic analysis of MenC should be enhanced to detected the emergence of specific clone and to establish relationship among national and /or international meningococcal strains.

Session III

COVID-19 LEGAL ISSUES

Chairpersons

Livia Besi, Felice Marco Damato, Roberta Tittarelli

CAFFEINE CONSUMPTION IN PROFESSIONAL, AMATEUR ATHLETES AND CADAVER, AS REPRESENTATIVE OF GENERAL POPULATION: TOXICOLOGICAL EVIDENCES, CO-USE OF OTHER SUBSTANCES AND POTENTIAL MECHANISMS OF DAMAGE

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In recent years, the risk of caffeine intoxication has increased due to the easy availability of analgesics, CNS stimulant medicine and dietary supplements at shops, health stores and e-markets. Even though, lethal cases from caffeine intoxications are quite uncommon.

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. Common features of caffeine intoxication, also known as “caffeinism” (i.e., a state of chronic toxicity from excessive caffeine consumption), include anxiety, agitation, restlessness, insomnia, gastrointestinal disturbances, tremors, psychomotor agitation, and, in some cases, death. Symptoms of caffeine intoxication can mimic those of anxiety and other affective disorders. The cardiovascular effects include supraventricular and ventricular tachyarrhythmia. The direct cause of death is often described as ventricular fibrillation.

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 consumption and co-use of other illegal substances in professional athletes, non-professional athletes and cadavers as representative of the general population; in the latter group, indirectly calculated from dosing caffeine levels from post mortem samples. We enrolled 123 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, 127 cadavers (aged < 50 years-old) has been selected from morgues of the center of Italy.

Thank to our study we would like to demonstrate that caffeine assumption 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.

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.

EFFECT-BASED METHODS FOR MONITORING AND ASSESSMENT OF AQUATIC ECOSYSTEMS

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Background. The application of effect-based methods is highly recommended for the detection of effects (e.g. genotoxic, neurotoxic) in the ecosystems caused by mixtures and chemical contaminants not included in the legislation; these methods (mainly bioassays *in vitro* and *in vivo*, biomarkers) can have an important role, as screening or early warning system for the monitoring programmes of surface waterbodies. Analysing, detecting and quantifying all the chemical substances in the aquatic environment is very challenging and in the context of the common implementation strategy of the EU Water Framework Directive (WFD) these methods have been suggested. Furthermore the effects of water scarcity and flooding can modify the environmental fate of several contaminants in the ecosystems and the use of innovative tools in combination with chemical analyses can also support the identification of the sources of pollution.

Methods. In the first part of the project a review about the use of effect-based methods in Europe has been carried out and the potentiality to be implemented in the European and national legislation has been remarked; furthermore the possibility also to prevent effects on human health has been considered in the review. In the second part of the project some of these methods have been applied in the Tiber river basin, mainly in the urban part, 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 including urban waste water effluents, illegal landfills and wastes, diffuse pollution, small enterprises emissions. 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 bioassay with *Daphnia Magna*, the algae test and also eco-genotoxicity assays (e.g. comet assay).

Results. The results of the project have showed that there is the need to include these monitoring methods in the legislation because of their potentiality to detect effects relevant for the environment and human health. The application of these methods in the field (Tiber river basin) has confirmed the validity of this approach. In the Tiber river basin different ecotoxicological effects have been detected and the results can contribute to help the local authorities to apply the best measures to protect the aquatic ecosystem.

Conclusions. The results of this study, will contribute: 1) to improve the knowledge of the quality status of Tiber river and help to identify the sources of pollution 2) to define innovative monitoring methods to be included in the national and European legislation.

CORRELATIONS BETWEEN ROSCHACH AND WAIS-IV IN SUBJECTS WITH INTELLECTUAL DISABILITY

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Background. Wechsler Adult Intelligence Scale – IV (WAIS-IV) and Rorschach Inkblot Test are often included in diagnostic routines by many clinicians in order to measure the “Performance” from two different points of view; while the WAIS-IV is used to analyse intelligence and cognitive abilities, the Rorschach test evaluates how people respond to various standardized tasks. The administration of projective methods in subjects with a diagnosis of intellectual disability presents some issues related to the validity of the test and therefore the reliability of the results.

Methods. The sample of this study consisted in 25 records of outpatients with intellectual disability selected from the archives of Policlinico Umberto I Hospital’s clinical psychological assessment service. All the selected records had to contain the full administration of psychological assessment battery which including both the Rorschach test and the WAIS-IV; in addition, all the Rorschach worksheets have been coded using the Comprehensive system of J.E Exner. Multiple Spearman’s rank correlations were performed to determine whether there were significant association between WAIS-IV and Rorschach indexes. Furthermore, the total sample was splitted in two subgroups: the first was composed of subjects whose IQ scores falls in the WAIS-IV range of <69 points (N=19), while the second one was composed by those whose IQ scores falls into 70-79 range (N=5). N=1 case has been excluded because the subject wasn’t part of neither of the previous ranges of IQ. In order to analyse differences between groups a one-way ANOVA was performed.

Results. Rorschach’s Zd index (Z difference) reaches a strong negative correlation with both WAIS-IV Full IQ scale ($p < 0.01$) and Perceptual Reasoning Index (PRI; $p < 0.01$), while a moderate negative correlation was found with Working Memory Index (WMI; $p < 0.05$) and Processing Speed Index (PSI, $p = 0.05$). Another moderate correlation was found between S (White space responses) and PRI ($p < 0.05$). One-way ANOVA shows that the two subgroups only differ in S responses.

Conclusions. These findings suggest that Zd may not just be a factor which describes processing Efficiency, but it could describe a complex factor which also involves cognitive domains associated with Perceptual reasoning assessed within WAIS-IV. Regarding the findings on S responses, results are in line with the international literature.

REVIEW ABOUT APPLICATION OF LAW 24/2017 (GELLI) DURING THE FIRST THREE 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 professional 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. Moore 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 three 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. 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 provides important information supplementary to the traditional autopsy and prospect 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. PMCT allow to differentiate between normal post-mortem changes from heat-related changes and helps the pathologist in victim's identification and in localization of possible sites for collecting DNA/fluid samples.

Future perspectives. The main objective 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: 1. 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]. 2. 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 losing fluids during dissection]. 3. 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].

PATIENT SAFETY: CLAIMS ANALYSIS AND CLINICAL RISK MANAGEMENT

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Law 24 of 8 March 2017 (Gelli Law) introduces considerable innovations in the field of the qualification of care security and the implementation of risk management. From this recent framework, the need arose to test the utility of the analysis of litigation data in terms of monitoring and implementation of clinical risk management policies. Claims analysis consists in the review of all the documentation that includes medical records, medico-legal reports, judicial documents and sentences, allowing to collect a huge amount of data that can be used to qualitatively evaluate errors and adverse events. In addition, the data on closed claims provide economic assessments and may reveal important and previously unestimated aspects, such as information on latent errors and rare events: data that are not easily detectable by the single review of medical records or by observation.

This study aims to define, harmonize and group the concepts of safety of care in a standardized classification in order to improve patient safety.

A data collection model was created, inspired by the conceptual framework of the International Classification for Patient Safety (ICPS), suitably elaborated in relation to data of interest. This classification was applied to the analysis of all claims against the A.O. Policlinico Umberto I of Rome, from 2012 to 2019.

Data integration made it possible to obtain statistical information about the categorization of the type of event and the patient outcomes, and also a careful evaluation of the event in order to break it down to trace the causes and possible influencing factors. Finally, the processing of data allowed to obtain qualitative valuation, economic estimates as well as medico-legal assessments on the degree of deviation from Evidence-Based practices. The results obtained advise the value of a methodological approach in the correct management of litigation.

In conclusion, a reliable medico-legal model for the management of litigation has been obtained, with the creation of a standardized database that can make possible an accurate monitoring of claims, with assessments aimed at the objective of improving the quality of healthcare assistance, providing a valuable tool to increase patient safety and reduce exposure to claims.

REGULATION OF MIRNAS AS NEW TOOL FOR CUTANEOUS VITALITY LESIONS DEMONSTRATION IN LIGATURE MARKS IN DEATHS BY HANGING

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This study aims to demonstrate that the application of miRNA expression in forensic pathology, in cases of hanging, applying the method on skin samples. The proposed investigative protocol allowed us to highlight a different miRNA expression in the skin ligature marks of subjects who died by hanging compared to healthy skin control samples.

A total of 36 skin samples from ligature marks and 28 samples from non-injured skin of subjects who had died by suicidal hanging were analyzed.

In all cases of hanging, sections of skin were removed from the neck at the site of the greater depth of the marks. In control cases skin samples were taken from the anterior face of the neck.

A immunohistochemical investigation of skin samples was performed utilizing antibodies anti-tryptase, IL-15, CD 15 and Troponin-I fast skeletal.

Immunohistochemistry showed a patchy dermal strong positivity of CD15 (++++), tryptase (++++), intracytoplasmic depletion of Troponin I appreciated in cervical muscles (++++), and IL-15 (++++), reaction in the marginal zones above and below the hanging marks.

The results obtained showed an increase in the expression of miRNAs recognized as regulators of the inflammatory response in skin lesions such as miR125a-5p and miR125b-5p. Furthermore, overexpression of additional miRNAs – miR214a-3p, miR128-3p, miR130a-3p, and miR92a-3p – with anti-inflammatory activity was highlighted. It was possible to document a statistical significance to control skin samples only for miR103a-3p ($p < 0.05$), miR214-3p and miR92a-3p ($p < 0.01$) The upregulation of miR222-3p and miR150-5p, respectively related to mast-cell activation and neutrophils after the application of traumatic stimuli supports the immunohistochemical data showed in literature. The diagnostic accuracy of miRNAs could expand the range of diagnostic tools available in the assessment of the vitality of a lesion.

EXHUMATION OF UNIDENTIFIED BODIES AT THE CEMETERY OF ROME: ONGOING IDENTIFICATION

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According with a protocol developed by the Ministry of Interior, starting from 2017, 12 unidentified bodies at the Cemetery of Rome were exhumed with the intent of properly collect *post-mortem* data, anthropological and odontological analysis, and biological sampling. Since some of them had soft tissues and some were skeletonized a different approach was necessary.

A traditional osteological approach was used for the skeletonized human remains as for virtual CT dental and bones analysis for undecomposed bodies. The anthropological profile was developed including ancestry, sex, age, stature as well as dental characteristics, personal belongings and any other potentially useful information. All the data of the previous body recovery were searched in the Court Archives and the information were used to seek a missing person list for a possible identification. In two cases, missing persons match these profiles.

A body originally found in the river in September 1998 was coherent with a woman missing since August 1998. Although neither *ante-mortem* radiographs nor medical records were found, the family produced pictures and very detailed descriptions about characteristic and dental work. All the data between the unidentified body and the missing person matched and were sufficient for a positive identification. Conversely, DNA analysis from the exhumed bones resulted in degraded genetical material despite of several attempt of extraction.

A body dismembered by a train was matching with a man missing since 1993. In this case DNA analysis is still in process.

Files belonging to some cold cases of unidentified bodies were also analyzed and in 2 cases a possible match was investigated. Bodies were not exhumed and the anthropological profile was made using original pictures and documents from previous recovery and autopsy. The final identification was confirmed comparing DNA sample collected at that time.

These cases confirm that the odontological identification is effective, quick, and reliable when both sufficient qualitative and quantitative level of data can be retrieved, even if there is absence of radiographic material. In this case, a wide investigator experience is required. In the other hand, in case of decomposed cadavers, due to the costs and time required, DNA analysis should be considered the last option, in case of failure of previous methods.

SUDDEN CARDIAC DEATH (SCD): LOOKING FOR PREDICTIVE GENETIC MARKERS

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Background. SCD constitutes one of the most important unsolved challenges in forensic pathology because of the failure to determine the exact cause of sudden death. Impact of genetics and genetic testing on clinical management of these diseases is unquestioned. In particular, genetic tests are an important tool for identifying pre-symptomatic individuals carrying genetic variant that predisposes them to SCD. Project aim is to clarify the role played by two SCL6A gene polymorphisms as a "trigger" in SCD or even as indirect factors for subjects addicted to drugs abuse. Molecular investigations will lead to clarify whether subjects using "smart drugs" are genetically predisposed and this investigation will be carried out in both competitive and non-competitive athletes, in order to identify the possible role of genetic polymorphisms in doped subjects.

Expected (or preliminary) Results. In this experimental study, male rats will be divided into mature and immature rats. Mature rats were 8 weeks old and immature rats were 4 weeks old. Forty mature male rats weighing between 200 ± 10 gr and forty immature male rats weighing between 90 ± 5 gr were randomly selected from the laboratory animal center at Catania University. The animals were housed individually in an air-conditioned room (12 hrs. dark/12 hrs. light) at $23 \pm 2^\circ\text{C}$ and had free access to tap water and standard food pellet. All animal experiments were conducted in accordance with national guidelines and protocols, approved by the Institutional Animal Ethics Committee (IAEC no.03/028/07). 40 mature rats were divided into 4 groups: group A and B, received 10 mg/kg/day ND interaperitoneally (15) for 35 days and 70 days, respectively as short and long term groups. Group C (control group), received normal standard diet, but did not receive any treatment, and group D (vehicle group), received a DMSO solution in two periods, 35 and 70 days. 40 immature rats were divided like mature ones. The ND doses were selected on the basis of reports of nandrolone decanoate use in human. And, period of administration mimics one cycle of AAS abuse by athletes. 48 hours after the final drug administration, body weight was measured and the rats were killed rapidly under anesthesia followed by cervical dislocation. Heart will be dissected and preserved in liquid nitrogen or embedded in paraffin for morphological and molecular evaluation.

Future perspectives. Primary study aim is to identify genetic markers predictive of SCD trying to find miRNAs that are differently expressed in genetically predisposed subjects. The histopathological examination of the heart will be carried out on 30 rats.

POST-MORTEM CARDIAC-MAGNETIC RESONANCE (PMCMR): A NOVEL DIAGNOSTIC TOOL IN ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY (ARVC)

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Background. Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) is a genetic disorder inherited in an autosomal dominant (in up to 50 % subjects) or autosomal recessive pattern, with a penetrance of 20-35% and an estimated prevalence of 1-5:1,000 in the general population. ARVC is characterized by fibro-fatty myocardial replacement and ventricular arrhythmias, and is a main cause of sudden death in young people (20% of all cases in subjects < 35 y.o.). In particular, sudden death may be the first manifestation of ARVC, with the diagnosis made by autopsy investigation.

Methods. We report on 5 cases of sudden death occurred in apparently healthy subjects (3 males and 2 females, age 34±SD 18.73 years) with no history of cardiac disease, examined by complete standard autopsy. A toxicological screening was performed in all the cases. During the autopsy the heart was fixed with 10% buffered formalin solution. After 2 weeks, a PMCMR on *ex-situ* formalin-fixed heart was performed with a 1.5 T clinical scanner (General Electrics Healthcare, Milwaukee, Wisconsin, USA) using a quadrature bird-cage multichannel coil. The PMCMR protocol included a whole heart 3D-SSFP (3D-FIESTA) acquisition with the following parameters: slice thickness 1 mm (interpolated to 0.5 mm), NEX 1, FOV 19 cm, matrix 512 x 512, 60° flip angle, TR/TE equal to 8.4/4.1. FSE images with the following parameters were also acquired: slice thickness 2 mm, NEX 1, FOV 32 cm, matrix 256 x 256, 90° flip angle, TR/TE equal to 840/8.1. Macroscopic and microscopic examination (hematoxylin-eosin, Masson's trichrome, Van Gieson, Red Congo and Perls' stainings) of the heart was then performed.

Results. At autopsy, the gross examination of the heart and of other organs and tissues was essentially negative in 2 cases, while in the others yellowish areas of fat infiltration were evident. Conversely, PMCMR showed in all the cases scattered areas of fibro-fatty infiltration in right and/or left ventricle, and guided the specimen sampling for histology, that revealed fatty tissue with sparse isolated myocardial cells or strongly disorganized clusters of myocardial cells trapped in fibrous tissue, including degenerating myocyte

Conclusions. PMCMR of *ex-situ* formalin-fixed heart is useful for the detection of cardiac alterations, that may be missed by macroscopic examination, and can be proposed as a guide for histological analysis in the cases of juvenile sudden death.

THE FEAR OF THE UNKNOWN: THE IMPACT OF COVID-19 LOCKDOWN ON THE USE OF LEGAL AND ILLEGAL PSYCHOTROPIC SUBSTANCES

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On 31 December 2019, China reported to the World Health Organization (WHO) the detection of a cluster of atypical pneumonia cases with unknown etiology. On 12 January 2020 the genetic sequence of SARS-CoV-2 (COVID-19) was identified: at that time, no one could have predicted the dramatic changes that the discovery of a new coronavirus would have brought worldwide. On 11 March 2020 the WHO announced the COVID-19 pandemic diffusion and to further reduce the transmission of the virus, many countries adopted physical and social distancing exceptional measures. Closure of non-essential stores, excessive exposure to information on social networks and media platforms, prolonged periods of isolation and the fear not being able to support their own family: what were the effects of the lockdown on the physical and mental health of billions of people forced to withdraw from work and loved ones? Stress, sleep disorders, depression, anxiety and post-traumatic symptoms were only some of the trauma caused by the pandemic. Beer, spirits and wine sales have dramatically risen worldwide: the number of alcohol poisoning cases increased in several countries, also due to the mistaken conviction that alcohol would have protected them from COVID-19 infection. The growing concern for the uncertain future has been strictly related to the rise of antipsychotics consumption. Data gathered worldwide during indicate that the number of weekly prescriptions for antidepressant, anti-anxiety and anti-insomnia medications increased since the COVID-19 outbreak. Although the pandemic caused global restriction in living and traveling, the illegal drug market didn't disrupt its activities. The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) reported the growing number of illegal drugs seizures in many EU countries: an adaptation of trafficking routes and concealment methods together with an increase in the use of the darknet markets for drug sourcing were also observed. The illegal cannabis products market have not been disrupted by the pandemic: before the restrictive measures were enforced, a peak in demand was registered, maybe due to the stockpiling activity of the users. Concerning cocaine use, to an initial decrease caused by the closure of naval and air routes, an increase in its consumption was observed. The heroin use remained stable despite the prices rise reported by several EU countries. Conversely, the closure of pubs, discos and the cancellation of music festivals caused a request diminution for synthetic drugs (as amphetamine, MDMA, methamphetamine) and New Psychoactive Substances (NPS). The economic and social consequences of the current crisis associated to a high unemployment rate necessarily affect the rise of illicit drugs, alcohol and antipsychotics consumption. Preliminary evaluation of available data, despite the short observational period, represents a source of serious concern and demonstrates the need of improved action to protect public health in the COVID-19 era.

TOXICOLOGICAL AND LEGAL ASPECTS ON ROAD SAFETY

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Road safety is a widely discussed topic and several attempts to reduce accidents and even deaths have been made by institutions in recent years. Unfortunately, statistics have not always been positive and, as recommended by the former Minister Marco Minniti in 2017, a new boost is needed in contrast activities to the most dangerous driving behaviours. In particular, Driving Under the Influence of Drugs (DRUID) is still a key phenomenon for road safety. This research project aimed to study this phenomenon in order to i) obtain a wide comprehension of its magnitude and ii) plan and implement protocols for management of forensic toxicological analyses in compliance with the Italian road safety laws (articles 119, 186, 186-bis, 187 c.d.s. and art. 589-bis and 590-bis c.p.). For this reason, my research activity was focused on i) the relevance of DRUID phenomenon and on ii) the evaluation of already available protocols. In particular, the epidemiological study was conducted on the basis of the data provided by the Forensic Toxicology Division of the University of Florence, where several analytical protocols have already been adopted. Since 2018, over 3,000 analyses have been performed. Most of them were carried out for driving licence purposes (such as renewal and regain). In these cases, cocaine was the most prevalent illicit drug, followed by cannabinoids and opiates. Methadone and amphetamine were found in a few cases. Benzodiazepines were the most consumed prescription medications. Alcohol was the most relevant substance in road traffic accidents. None of the new psychoactive substances were detected. Correlation among gender, age, job and drug consumption were also evaluated. Beside the epidemiological study, a final result of my research activity will be the proposal of protocols for the toxicological analyses in compliance with the Italian laws on road safety. These protocols will provide information and instructions on all the aspects of forensic toxicological analyses in this field, representing a valuable tool for the various stakeholders (Law Enforcement Agencies, National and Regional Institutions, Health-care and forensic laboratory personnel).

Session IV

The impact of the COVID-19 pandemic on human rights

Chairpersons

Giulia Civitelli, Giulia Marchetti

GENDER DIFFERENCES AND OCCUPATIONAL FACTORS FOR THE RISK OF OBESITY IN THE ITALIAN WORKING POPULATION

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Background. Obesity is a multifactorial condition and a major risk factor associated with several non-communicable diseases, such as cardiovascular disease, and with a higher risk of premature death and disability. Sex-specific factors have key roles and must be taken into consideration in studying occupational factors associated with the risk of obesity. The aim of this study was to investigate gender differences in Body Mass Index (BMI) in a large cohort representative of Italian workers and, correlating this index with several demographic and occupational variables, to verify sex- and work-dependent differences in the risk of obesity.

Methods. We utilized data from INSuLa, a cross-sectional, nationally representative survey of the Italian worker population conducted in 2013 by the Italian Workers' Compensation Authority to investigate health and safety at work. Analyses were run on a sample of 8000 Italian workers, aged from 16 to 64 years. Logistic regression models were employed to assess gender differences in the relation between occupational characteristics and BMI. We adjusted for age, education, variables related to health protection at work, and chronic conditions and diseases.

Results. There were several significant differences in the BMI between males and females, linked to some occupational factors. For instance, female shift workers were 1.32 times (95% CI 1.11–1.57) more likely to be overweight or obese than non-shift workers, and this association was maintained when controlling for confounders. The likelihood of overweight or obesity among women who worked 1–2 night shifts per week was significantly higher – 1.5-1.6 times – than those on day shifts.

Conclusions. Gender-specific differences in occupational factors associated with the risk of obesity are useful with a view to characterizing this risk and helping identify workplace-targeted intervention strategies.

INTEGRATING CLIMATE AND ENVIRONMENT PUBLIC DATASETS IN SURVEILLANCE FOR EARLY WARNING

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Background. Surveillance and control of arboviral infections benefit from a One Health approach and cross-sectorial strategies, and this is central to the MediLabSecure Project, funded by the European Commission (DEVCO: IFS/2018/402-247). In particular, the Public Health team developed a survey on early warning surveillance, to identify the collection and use of surveillance data in the three sectors involved in surveillance activities (vector, human and animal) in the 22 countries of the Network (Albania, Algeria, Armenia, Bosnia and Herzegovina, Burkina Faso, Egypt, Georgia, Jordan, Kosovo, Lebanon, Libya, Mali, Mauritania, Montenegro, Morocco, Niger, Palestine, Rep. of North Macedonia, Senegal, Serbia, Tunisia, Turkey). It was also investigated the awareness and utilisation of global public datasets in early warning activities, given the acknowledged impact of environment and climate on arboviral infections.

Methods. An online questionnaire was developed using Google Form© and 110 officially appointed national contact points, belonging to the mentioned sectors of the study area, were invited to answer. One question asked if the respondent's office had access to any global public dataset related to Climate & Environment and, in case of "yes", an additional question asked to which one/s, and for which purpose. From May until December 2019, responses were collected and then analysed.

Results. Overall, 81 completed questionnaires were received. In half of them (41/81, 50%), it was stated that they do not use global public datasets; in the 30% (24/81), that they do not know, and only in the other 20% (16/81) global public datasets are in use. Within each of the three sectors, the users correspond to about the 20% of the respondents: 4/20 for the vector sector, 6/30 and 6/31 for the human and animal sectors respectively. Furthermore, 10 answers to the following questions were registered: seven reported the parameters investigated through the dataset and/or the purpose, and three reported examples of websites/platforms for global public datasets consultation, National or International.

Conclusions. The questionnaires highlighted a low level of use of global public datasets on climate and environment in the investigated study area, where only few respondents were able to produce examples of datasets in use. It appears important to implement awareness of their availability with a One Health approach, in order to strengthen integrated early warning strategies in the three involved sectors.

GLOBAL HEALTH EDUCATION IN ITALIAN UNIVERSITIES

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Background. Global Health Education (GHE) is spreading in Europe and in other parts of the world. Since 2008, Italian Universities have offered activities to medical and other health profession students related to Global Health (GH), which is grounded in the theory of social determinants of health and inspired by social justice. The educational activities included elective courses as well as community and service-learning experiences, referred to as GH gyms. An attempt of measurement of the long-term impact of educational experiences offered by Sapienza University has been carried out, together with a survey on the availability of those experiences at national level.

Methods. To assess the impact of GH educational experiences offered by Sapienza, a questionnaire was elaborated and validated. It was sent to participants by e-mail. Quantitative results were analysed through descriptive statistics and qualitative answers were carefully read and classified. To evaluate the offer of those educational experiences at national level, a survey was carried out using a questionnaire administered to a network of interested people, with different roles in the academic world: students, professors, the Italian Network for Global Health Education. The features of courses were analysed through a score.

Results. A total of 758 students from different faculties took part to the educational experiences. Only 488 e-mail addresses were available. One hundred and five (25.1%) questionnaires were returned. Participation in GH gyms was perceived to have had a higher influence on future professional and personal choices, when compared to participation in elective GH courses. The national survey showed the presence of GH educational proposal in the country, mainly elective, with a significant difference in the quality of the courses.

Conclusions. Consideration of health and social issues related with inequities in health and the use of interactive teaching methodologies had important effects on social responsibility of a large number of students. The inclusion of global health education in health and social curricula and the use of interactive methodologies with a correct evaluation of results are the indications that emerge from this research, together with the necessity of a strong involvement of students and professors. Some work has been done at national level, but a higher and more specific commitment is needed to insert GHE in mandatory curricula of health courses.

MASS SPECTROMETRIC SPECIFIC DETECTION OF POLYCYCLIC AROMATIC HYDROCARBONS (PAH) IN GC/MS-NCI WITHOUT USING AUXILIARY IONIZATION GAS. A METHOD FOR THE ANALYTICAL DETERMINATION OF PAH CORRELATED WITH THEIR CARCINOGENICITY

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Background. Some organic compounds, present in the environment in traces and ultra-traces and difficult to determine because dispersed in matrices that cause interference, can create serious problems for human health because of their carcinogenic potential. The toxic effects but also the investigation methods are linked to their structure-activity relationship. For carcinogenicity, the IARC has defined 10 characteristics, called Key Characteristics (KC), that all human carcinogens have in common. The first KCs link the carcinogenic potential of a species to its electrophilic power which could be characteristic or be induced by the metabolic activation that leads to the formation of adducts with DNA. The aim of this project is to study the electrophilic power of the main organic micropollutants starting from the Polycyclic Aromatic Hydrocarbons (PAHs) and then the Polychlorobiphenyls (PCBs), the Polychloro-p-Dibenzodioxins (PCDDs) and Polychloro-Dibenzofurans (PCDFs) by gas phase reactions of different species of electron donors. The evaluation of the correlation between the toxicity factors of each organic micropollutants and their predisposition to ionize in Chemical Ionization (CI) was carried out using different instrumental settings (source GC/MS) according to the reagent gas.

Preliminary results. Hydrogen was selected as the best gas to evaluate the electrophilic power of PAHs and to obtain a selective GC/MS method applying negative chemical ionization modality for detection. Hydrogen itself acts as ionization gas, which provides an extraordinary specificity for some isomers. The GC runtimes are shortened without losing column efficiency, which ensures a cost-effective, rapid and reliable method. Distinct sets of congeners among PAHs have been in order to depict environmental pollution. There is a list of 16 priority PAHs according to USA-EPA whose seven are identified as carcinogenic (cPAHs). A mass spectrometric method based on NCI was obtained, with no need to dampen the external ionization gas for the specific analysis of cPAH. The other PAHs that are not classified as carcinogenic do not respond in this ionization.

Future perspectives. The results required for PAHs will be extended to other organic micropollutants. If a correlation between the POPs factor response in the formation of GC/CI-MS adducts and electrophilic DNA is demonstrated, it could be extended to other known and unknown chemical species in industrial emissions and in ambient air. This could aid mechanistic study in the formation of electrophilic DNA adducts. This means taking into account substances whose toxicity has however been underestimated despite their not negligible concentrations.

IMMUNIZATION CHALLENGES TARGETING NEWLY ARRIVED MIGRANTS

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Background. Migrants represent a potential vulnerable group and adequate health assistance, including vaccine preventable diseases prevention, should be ensured. The Istituto Superiore di Sanità launched a survey with the aim of investigating immunization policies and practices 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 between January and 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 countries and 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. Vaccinations are mainly given at holding and/or community level and only 5 countries vaccinate at entry level. Fourteen countries have procedures to ensure migrants' access to vaccinations at the community level (e.g. vaccination services/health workers/GPs/paediatricians) if vaccinations are not previously delivered at holding level. Information on delivered vaccines is recorded for children/adolescents in 22/28 countries and for adult migrants in 19/28 countries. Methods for recording information (paper or electronic register/electronic database/paper archives) differ greatly between countries and only an individual vaccination card is given to migrants in most countries. In 13 countries individual data are not made available or transmitted from the sites where vaccinations are delivered to any other centre/institution and in 15/28 countries aggregated data are also not made available. Data about migrants' compliance to vaccination are not collected in 20/28 countries.

Conclusions. The results show that policies regarding migrants' immunization are available in most of EU /EEA countries. On the other hand, practices to ensure vaccinations to migrants are scarcer and more problematic, also due to lacking documentation of previous vaccinations. Few countries have operative procedures, in many there is poor collaboration between health institutions and reception centres, and recording and transmission of immunization data are not widely spread. This survey could be the first step to analyse the situation and the gaps in the countries taking in mind that, due the migrants' mobility, it is important to share data within and across countries to better respond to migrants' immunization needs.

NATIONAL MONITORING SYSTEM FOR PATIENT SAFETY IN ITALY, CONSENSUS BASED APPROACH AND DATA SOURCES INTEGRATION

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In 2017 the Italian national legislation on patient safety instituted the National Observatory for patient safety with the participation of the national institutions (Agenas, AIFA, CSS, ISS, Ministry of Health), regional health authorities, and national experts. The aim of the National Observatory is monitoring the Adverse Events (AEs), near misses and the main risks associated with healthcare provision and providing national guidance to improve patient safety. With this aim, the Observatory projected and realised a national monitoring system addressing the following fields of interest of patient safety: governance of safety, Healthcare-Associated Infections (HAI), Antimicrobial Resistance (AMR), surgical procedures, medication safety and transfusion.

Registries of indicators computable from 30 data sources available at the national level were realised for each field of interest considered. Groups of national experts were created for each specific field of interest. To select a set of core indicators, national experts assigned a score from 1 to 9 to 6 criteria to each indicator of the registry relating to their specific field of study.

Experts scored the following criteria: validity, reliability, relevance concerning the theme of safety of care, actionability, computability at a regional level and international comparability.

Based on the scores attributed by the experts for each criterion, specific combined-scores of indicator quality and variability among experts “evaluation were computed. The indicators scoring above a particular rating for quality and below a specific rating for variability among experts evaluation were considered for inclusion in the national monitoring system and further evaluated by the groups” coordinators.

Through the consensus approach, 67 indicators were selected from registries including totally 673 indicators. The chosen indicators were computed from 10 different data sources available at the national level. Data sources taken are the surveillance of antimicrobial resistance, the surveillance of bacteremias for Carbapenemase-Producing Enterobacteriaceae (CPE), the registries of medication consumption, the evaluation of the implementation of safety procedures, the public reporting of healthcare outcomes (PNE), the hospital discharge schedules (SDO), the incident reporting for sentinel event, the claims and litigation registry and the surveillance of transfusions. Moreover, the Observatory conducted an ad hoc survey to evaluate the level of implementation of incident reporting at a regional and local level. The national monitoring and evaluating system provided essential pieces of information concerning the safety of healthcare in Italy with particular focus on the governance of safety, HAI, AMR, surgical procedures, medication safety and transfusion

IMPLEMENTING HEALTH TECHNOLOGY ASSESSMENT FOR GENOMIC TECHNOLOGIES IN ITALY: NETWORK, PATHWAYS AND METHODOLOGY

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Background. As more genomic technologies become ready for implementation, a complete and well-structured process to guide their introduction into the clinical and public health practice is needed. In Italy, the inclusion of genomic technologies into the Essential Levels of Care is largely unregulated. Thus, our project aims to find structural, organizational and methodological solutions for their assessment and approval, in order to maximize population health benefits and the use of resources. Particularly, we aim to define a competence network, integrated procedural pathways and a comprehensive methodology for the Health Technology Assessment (HTA) of genomic technologies in Italy.

Methods. Six actions are in progress: 1. Creation of an Institutional Advisory Board with commissioning, consulting and supporting functions; 2. Analysis of the national legislation on HTA and genomic technologies, in order to identify existing actors, roles, pathways and networks; 3. Analysis of the HTA status in the Italian Regions, in order to identify organizational differences; 4. Systematic review of the literature, aimed at identifying and comparing the existing theoretical HTA frameworks for genomic technologies; 5. Consultation with the main national (RITHTA – The Italian network for HTA-) and international (INAHTA - The International Network of Agencies for Health Technology Assessment) networks, aimed at retrieving and analyzing actual assessment reports on genomic technologies; 6. Expert interviews to support the development of a comprehensive HTA methodology for genomic technologies.

Results. Preliminary results are available for actions 2 and 3. Action 1 was suspended because of the COVID-19 emergency while actions 4, 5 and 6 are still being planned. The analysis of the national legislation retrieved five crucial documents related to HTA and genomic technologies in Italy; these documents define the central actors (The Ministry of Health, The Italian Institute of Health, and The National Agency for Regional Healthcare Services), their roles (with some inconsistency between the documents) and the main phases of the HTA process (priority setting, assessment, and appraisal). The analysis of the HTA status in the Italian Regions pointed out that 13 Regions have a specific regulation for HTA and that many differences exist across Regions in terms of technologies evaluated, methodology used, type of reports, etc.

Conclusions. The main barriers to the completion of the project goals might be the inconsistency about roles and responsibilities for the HTA of genomic technologies, as emerged from the analysis of the national legislation, and the organizational differences existing between the Italian Regions.

ASSESSMENT THE SOCIAL IMPACT OF SUBJECTIVE STRESS IN DIFFERENT WORK POPULATIONS COMPARED

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Background. The European Agency for Safety and Health at Work defines work-related stress as a condition that "occurs when the demands of the work environment exceed the ability of workers to cope with it". The evaluation of work-related stress is a legal requirement under the Legislative Decree 81/08 s.m.i., and generally is carried out by the employer jointly with the RSPP and doctor. The aim of the study is to evaluate subjective stress through the use of a 35-item "questionnaire-indicator tool" developed by INAIL, in 1244 subjects: 363 VDU operators, 150 childhood school teachers, 302 kindergarden teachers, 257 cleaning operators, 122 rescuer drivers, 50 social workers. The questionnaire evaluates 35 items concerning working conditions considered to be potential causes of work-related stress corresponding to seven risk factors or organizational dimensions defined by the "Management Standards" model.

Results.

1. Demand Area. The purpose of the application fell in the green area for VDU operators. For teachers, educators, cleaning operators, and rescuer drivers the purpose of the application fell into the red area. while social workers are in the yellow area.
2. Control Area. The purpose of control fell in the blue area for the VDU operators, teachers and social workers, For those in charge of washing and cleaning, the purpose of the check fell into the red area, while for rescuer drivers it fell back into the yellow area.
3. Managers Support Area. The area of support from the superiors obtained an overall score in the blue area VDU operators. The cleaning and washing workers, the childhood school teachers, the kindergarten teachers and the rescue drivers have obtained a score the green area while social workers have obtained a score the red area.
4. Peer Support Area. This area has obtained an overall score the green area.
5. Quality of Relationships Area. This area has fallen into the green area for VDU operators. For cleaners and caretakers, social workers, rescuers, educators and teachers this area was particularly critical, the red area.
6. Definition of the Role Area. This role has obtained an overall score the green area for childhood school teachers, kindergarten teachers, rescuer drivers and cleaners. On the other hand, for social workers and VDU operator his area fell into the blue area.
7. Change Area. This area the total workers has obtained an overall score the green area, only social workers fell back into the red area.

Conclusion and perspectives. From the results of this survey, I would like to highlight any working and social factors that demonstrate the greatest cause of stress for workers.

DETERMINANTS OF ADHERENCE TO ART IN HIV+ WOMEN ENROLLED IN PMTCT PROGRAM IN WEST AND NORTH REGIONS OF CAMEROON

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In 2018, according to UNAIDS estimations, 62% (47-74%) of People Living With HIV (PLWHIV) worldwide are on Antiretroviral Therapy (ART), with a higher coverage among HIV-positive women (68% on ART) and 82% of pregnant HIV women having access to antiretroviral drugs to prevent the vertical transmission. However, the success of the fight against HIV programs does not depend exclusively on the availability of ARTs, but on retention in care and adherence to ART. The use of ART has been proposed worldwide by the WHO for the Prevention of Mother-To-Child Transmission (PMTCT) of HIV since 2012. The aim of this study was to highlight the determinants of adherence to ART for HIV + women of childbearing age, enrolled in HIV-PMTCT programs in the West and North Regions of Cameroon. A descriptive and analytical cross-sectional study was carried out from February to September 2019 in three treatment centers of PLWHIV, belonging to health districts in the West region (Bafoussam Regional Hospital and Dschang District Hospital) and the North region (Garoua Regional Hospital) of Cameroon. Data were collected using a questionnaire administered face to face and then analyzed using SAS version 7.8 software. Statistical significance was set at $p = 0.05$. To identify the determinants of adherence to ART, a multiple logistic regression analysis was performed.

A total of 1,000 women were enrolled. The mean age of the participants was 17 (± 2 SD) years. Concerning the civil status, 44.6% ($n=446/1,000$) of participants reported to be single, whereas 47.6% ($n=473/994$) were married, with 52% ($n=404/777$) being in a polygamous household. Overall, the prevalence of the adherence to ART was 68.6% ($686/1,000$). The unshared serological status with the spouse (OR=0,360, $p=0,0075$), the unknown ongoing ART by the spouse (OR=0,177, $p<0.0001$), the spouse's HIV status (OR=0,413, $p=0,0087$), the daily frequency of ART (OR=0,204, $p<0.0001$), and the knowledge of the risks of non-adherence to ART (OR=0,149, P value<0.0001), have been identified as negatively influencing women's adherence to ART. However, the higher level of education (OR=1,691, P value<0.0001), and the fact to having more than one child (OR=2,588, P value <0.0001) were influencing positively women's adherence to ART.

The study shows that, there are many determinants influencing the adherence to ART among women enrolled in HIV-PMTCT programs in Cameroon. To reduce considerably the mother-to child transmission of HIV, strategies should be adopted to control these determinants in order to reach the 90-90-90 goal as advocated by UNAIDS.

NEW SYNTHETIC OPIOIDS: DEVELOPMENT OF ANALYTICAL METHODS FOR THEIR CHARACTERIZATION AND QUANTIFICATION BY MEANS OF (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 730 compounds have been identified by the European Monitoring Center for Drugs and Drug Addiction (EMCDDA). In this context it is of significant importance to have the right tools to identify the most recent NPS and verify their consumption. Among the newest NPS, 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.

Methods. 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 their determination in different biological matrices, with a focus on fentanyls. Thanks to its high versatility and performances, UHPLC-HRMS/MS has been used as the analytical technique for the characterization, identification and quantification of target analytes.

Results. Two new NPSs, 4Fluoro-FuranylFentanyl and IsobutyrylFentanyl, found in seizures were characterized by UHPLC-HRMS and their structure was confirmed by NMR. In order to predict their metabolites *in silico* and *in vitro* studies were performed, while *in vivo* studies are in progress. To date, we have been able to identify several putative metabolites of the two new opioids. An analytical method for the extraction of these analytes in different biological matrices was developed and validated. The method involves the use of a small amount of biological sample (100 μ L of urine or oral fluid) which are treated with Micro Extraction by Packed Sorbent (MEPS) in order to clean-up and concentrate the sample. Analyses were performed by means of an UHPLC-HRMS/MS method previously developed.

Conclusions. The characterization of new synthetic opioids is of paramount importance to hinder their uncontrolled diffusion. In addition to discriminate the active use of the substance from a false positive, the knowledge of the drug's metabolic pathway is important. *In silico* and *in-vitro* methods provide useful information however *in vivo* studies are crucial to confirm the data; the development of the extraction procedure from urine and oral fluid will be used to identify metabolites at that stage.

THE EVALUATION OF PALLIATIVE CARE AND THE NEEDS IN PRIMARY HEALTH CARE IN THE CITY OF VLORE

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Background. The study of the needs of cancer patients is fundamental in order to build models where the service is adopted to the needs of the patients and is accessible for everybody. The management of these patients requires multidisciplinary approach closer to the patients and their needs, based on the law for palliative care in primary health care.

Methodology. This is a cross sectional quantitative study, based on the data of 3 questionnaires filled from cancer patients, members of community and health care personnel in the Vlore city with the following instruments:

- Patient/client experiences - patient questionnaire.
- Community Awareness of Palliative Care- CHSD.
- Palliative Care providers.

Results. From the experience of 100 patients was concluded that 67 % of them had severe or very severe pain, 71% were severely affected by other symptoms, 84% of the family members were very concerned of the situation, 42% did not have any information and 62% had unresolved issues.

92 family members or friends of patients filled in the questionnaire of “Community Awareness of Palliative Care”, mean age of 41 years old, from them 35% never heard of palliative care, 50% had no knowledge. 73% stated that this service does not meet the community needs, 74% did not get the needed support, 36% need basic care at home, 26% need day care for the sick, 24% need the help of volunteers. As for community needs people require home care (25%), qualified staff (9%), specialized centers and psychological services. 62 nurses of primary care with mean age 38.5 years we concluded that 36% did not have any training for palliative care, 50% learned this skill in practice. They say that they need more basic instructions on death process (53%), effects of certain meds (31%), pain management (23%), during the terminal delirium (39%), terminal dyspnea (31%), for nausea and vomiting (16%) and constipation (20%).

Conclusion. The data show that the palliative care in primary health care still does not function, the patients and the community members relate to many unresolved issues and the nursing staff needs to be trained in this area. It is necessary the implementation of a training program for the medical staff.

New research topics

FORENSIC APPLICATION OF MONOCLONAL ANTI-HUMAN GLYCOPHORIN AN ANTIBODY TO ESTABLISH VITALITY OF THE INJURIES

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Background. Glycophorins are an important group of Red Blood Cell (RBC) transmembrane proteins, playing a pivotal role in cellular biology. Monoclonal antibodies against Glycophorin A antibody (GPA) are employed in immunohistochemical staining during post-mortem examination: through this method, it is possible to point out the RBC presence in tissues.

Objectives. This project aims to investigate anti-GPA immunohistochemical staining in order to evaluate the vitality of the lesion both on bones and on soft tissues sampled from corpses in different decomposition state. This data could support the forensic pathologist in the resolution of not unequivocal interpretation cases, such as differential diagnosis between hanging and suspension of a corpse.

Preliminary results. 6 case were selected analyzing the documentation of all autopsies performed by the Institute of Legal Medicine of Rome from 2010 to 2019: 4 samples of fractured bones (cranium, vertebra, mandible, and rib) and 3 samples of soft tissues (soft tissue of larynx, skin in the neck region, and retina). For the control case the fracture region of the femur has been sampled. Monoclonal antibodies against GPA resulted positive in all analyzed cases, indicating the presence of RBC and demonstrating the vitality at the moment of the lesion. Indeed, the results in the control case have been negative.

Future perspectives. The preliminary results mark the importance of the GPA immunohistochemical staining to highlight signs of survival. Moreover, this study suggests that the use of this technique should be routinely applied in cases of corpses with advanced putrefaction phenomena, even when the radiological investigation is performed, the macroscopic investigation is inconclusive, and the H&E staining is not reliable. Though certainly not conclusive, this experimental application demonstrated that the use of monoclonal antibody anti-human GPA on bone fractures as well as soft tissues could be important to verify whether the lesion is vital or not and could be performed in not unequivocal interpretation cases.

ANISAKIS SIMPLEX S.L. AND THEIR INTERACTION WITH HUMAN CACO-2 CELLS

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Background. *Anisakis* is a nematode parasite of marine organisms characterized by a complex life cycle and humans, eating raw fish with infective larvae, can accidentally develop a zoonosis called anisakiasis. The larval mechanical action in the gastrointestinal tract and the release of excreted/secreted products and Extracellular Vesicles (EVs) can progressively determine hemorrhagic, erosive and ulcerous lesions, granuloma and chronic inflammation. Anisakiasis can be accompanied by mild or severe allergic symptoms ranging from urticaria, angioedema to anaphylaxis. Several studies characterized the parasite allergens and the associated Th2-mediated immune response resulting in the production of the IgE-mediated allergic reaction. However, the role of host's immune response during the infection and the potential implications are still unknown.

Objectives. The aim of this project is to develop a suitable in-vitro model to study *Anisakis*-intestinal cells interactions focusing on the host cell inflammatory response. Intestinal Caco-2 cell monolayers will be challenged with the alive Larvae (L) Crude Extract (CE) and exosome-enriched fraction (Evs). After 24 h of incubation cell supernatants will be tested for IL-8 and IL-6 production and cells will be tested for NF κ B and MAPK signaling.

Expected results. Previous studies on human dendritic cells, fibroblasts and cancer colonic cells have shown signs of inflammatory response, characterized by an induction of oxidative stress and an inhibition of apoptosis with an alteration in the expression of important cell cycle check points, as P53. Similarly, we expect that the parasite or its products can fine tune the expression of host inflammatory products in association with a potential alteration of intracellular signaling pathways.

Future perspectives. This study can highlight the pathogenic mechanisms that characterize the accidental interactions between *Anisakis* and humans, in order to study in deep eventual potential implications and consequences of the infection in the host as well as opening new ways for the identification of new diagnostic biomarkers.

CHEMICAL RISK RELATED TO AUTOPTIC AND MORGUE ACTIVITIES: ASSESSMENT OF WORKPLACE BIOHAZARDS TO IMPROVE HEALTH PROFESSIONALS' SAFETY

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Background. Among the risks associated with healthcare, diseases due to occupational exposure occupies a prominent position due to the extent of the risk, complexity of determinants and increasing epidemiological trend. The assessment of chemical risk represents an obligatory path in health activities from which health hazards could result due to exposure to chemical agents.

Objectives. Our proposal is a retrospective study on the working population of the autopsy room through which obtain clinical information about possible pathologies related to chemical agents (an in-depth study that goes back over the years of at least 15/20 years), from irritative problems (disinfectants) to more complex issues such as the possible occurrence of tumors

Expected results. The aim of the present study is the identification and characterization of the identifiable sources of chemical risk, as well as the identification and analysis of new sources of risk to which the different groups of professionals involved in performing the autoptic and morgue activities are exposed.

Future perspectives. The data emerging from the study carried out could highlight the importance of identifying the risks associated with the autoptic activities, as well as implementing preventive strategies aimed at reducing the exposure of professionals.

INSIGHTS INTO MALARIA TRANSMISSION TROUGHTOUT MOLECULAR STUDIES OF THE TRIPARTITE INTERACTIONS BETWEEN PARASITE, MOSQUITO AND HUMAN HOST

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Background. Malaria transmission between humans depends on parasite development and sexual reproduction in the mosquito vector that occurs in presence of gametocytes in the peripheral human blood. Human genetic background might drive the efficiency of parasite transmission to the mosquito and mosquito midgut represents the main bottleneck during *Plasmodium* life-cycle. So far, the mechanism of malaria transmission has been studied separately in the human host and in the mosquito vector: however, progresses in this field of malaria research are currently hampered by ethical, logistic and practical issues related to field and laboratory work. Alternative molecular approaches are needed to improve future studies focused on *plasmodium*-human-mosquito interaction and for the following development of new blocking malaria transmission interventions.

Objectives. We attempt to develop an innovative and sensitive molecular method to study, in one single infected mosquito, the interactions between the parasite, mosquito and human host. Our aim is to develop a Real Time PCR protocol to quantify ookinetes inside the mosquito and correlate this information with the specific human genetic background and with the immune response elicited in the mosquito midgut. To achieve this goal, we aim to dissect at molecular level *Anopheles coluzzii* mosquitoes infected with *Plasmodium falciparum* collected at different time-points post infectious blood meal.

Expected results. We expect to develop a molecular approach able to correlate the number of *Plasmodium* infecting ookinetes with both the human genetic background and the mosquito immune response. The parasite survival in the mosquito depends on the midgut immune response activation triggered at 24 h post infection, time frame corresponding to ookinetes passage through midgut epithelial layer cells. The ookinete number will therefore provide an evaluation of gametocyte abundance (gametocytemia) present in human blood, the main transmission index from human to mosquito. A list of marker genes known to characterize both ookinete stage and mosquito immune response will be tested. We will also analyze the expression profile of other genes, with the aim to find out new targets that could possibly describe the parasite passage in the mosquito, and be therefore useful in further studies directed to vector control and malaria transmission-blocking interventions.

Future perspectives. Future goals of the project will involve the application of this protocol in malaria endemic countries, through an analysis of wild single infected mosquitoes, thus investigating the contribution of specific human genetic conditions in malaria transmission. We hope that our work will provide a novel technical support in future field studies focused on malaria epidemiology and human host-vector-parasite interplay.

EPIDEMIOLOGY, RISK FACTORS AND OUTCOMES OF INFECTIONS CAUSED BY CARBAPENEM-RESISTANT GRAM-NEGATIVE BACTERIA IN PAEDIATRIC POPULATION

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Background. Infections caused by gram-negative resistant bacteria have increased worldwide but there are few available data for the pediatric population. In particular, Carbapenem-Resistant Gram-Negative (CR-GN) bacteria are an emerging global threat and are associated with high mortality and morbidity due to few therapeutic options.

Objectives. The objectives of our study are to describe the epidemiology, risk factors and outcomes associated to infections due to CR-GN in the pediatric population. Subsequently, we will use collected data to create an algorithm to predict the risk of CR-GN infection.

Expected (or preliminary) results. In this first phase we retrospectively collected data from the Paediatric Intensive Care Unit (PICU). We analyzed preliminary 65 patients, 32 presented a CR-GN infection due to: *A. baumannii* (16; 50%), *S. maltophilia* (3; 9.4%), *P. aeruginosa* (11; 34.4%), *K. Pneumoniae* (2; 6.2%). All isolates were multi-drug resistant, 13 (39.4%) isolates were sensitive to fluoroquinolones, 12 (36.4%) to aminoglycosides, 28 (84.8%) to colistin, 5 isolates were sensitive to tigecycline and 5 to piperacillin/tazobactam. Lower respiratory tract infections were the most frequent infections (20; 62.5%). At the univariate analysis we identified the following risk factors for CR-GN infection: age \leq 24 months ($p=0.004$), central venous catheter ($p=0.029$), urinary catheter ($p=0.024$), nasogastric tube ($p=0.001$), orotracheal intubation ($p=0.042$), mechanical ventilation ($p=0.042$), corticosteroids use in the previous 30 days ($p=0.048$) and at the time of infection ($p=0.040$), antibiotic therapy in the previous 30 days ($p=0.002$), in particular, carbapenems and glycopeptides ($p=0.011$ and $p=0.047$ respectively); length of stay in PICU before the infection ($p<0.001$); rectal colonization by carbapenemase-producing microorganism ($p=0.026$); *Candida* spp. infection in the previous 30 days ($p=0.010$). The length of hospitalization was significantly longer in the group of patients who had a CR-GN infection ($p<0.001$) and no fatal infections were observed.

Future perspectives. We are actually collecting data from a control group of PICU patients who did not develop an infection. We expect to enroll more patients to develop a decisional tree model to predict subjects at risk to develop GN-CR in order to implement prevention strategies.

TELEMEDICINE AND HTA: THE PATIENT AT THE CENTER OF THE EVALUATION PROCESS

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Background. HTA is a multidisciplinary assessment process that examines the short and long term consequences of using new or existing health technologies. Patients are directly involved as they live with the disease and know the fundamentals of treatments, side effects and benefits of drugs and technologies. Among the technologies being evaluated, telemedicine combines medical and IT techniques that provide remote distance care by eliminating the barriers of time, place and costs connected to accessing care. Telemedicine is used with great success in various fields and is very useful in the care of patients suffering from chronic diseases. In 2015 the first conceptual framework for the use of telemedicine during epidemics was published. This framework was subsequently updated for the implementation of telemedicine during the COVID-19 pandemic.

Objectives. The project aims to develop a patient involvement plan for the construction of HTA reports through the analysis of the scientific literature, the study of the organizational contexts in which telemedicine has been applied and evaluation of the response of patients that, in the Italian context, are treated both in hospital and territorial facilities. The effects of a treatment and/or benefits and advantages of drugs and technologies will be analyzed through targeted questionnaires on health status, quality of life and more specific aspects such as pain perception and adherence to therapies.

Expected results. The feedback from patients is essential to identify needs, requirements and gaps in health care and to provide a comprehensive view of the consequences of telemedicine use and its social, economic and ethical impact. In addition, the outcomes reported by patients will be essential to establish new clinical areas in which to implement telemedicine and work on strengthening existing ones, with the aim of ensuring the use of the best strategy for patient care. The published framework on the use of telemedicine during the COVID-19 epidemic could be used at scientific level to assess and describe the impact of telemedicine during epidemics.

Future perspectives. Telemedicine-based approaches to care allow for a bridge between different disciplines dealing with chronic patients, in particular public health and economics, and opens up new possibilities for research. To facilitate the acceptance of services by healthcare professionals and patients, it is necessary to train both recipients on the use of the new technology. The support of operating units and/or professionals trained in medical-scientific communication it will be essential to improve communication, care and assistance processes.

FAMILY AND COMMUNITY NURSING: A SOCIAL-HEALTH SERVICE REVOLUTION

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Background. The Family and Community Health Nurse (FCHN) is gathering a growing importance in primary health care and in enhancing public health resilience. This figure allows integration and interaction between social-health services and all the community-based healthcare workers. The increase in aging and the burden of chronic diseases around the world stresses the need of a shift in the way of thinking healthcare services improving the community setting and the family care in patients' home. Nursing care is the joining link between all the professionals working in community setting and the patients who are placed at the center of the whole care process. Therefore, new frontiers are opening up to develop this joining link by studying the FCHN figure, so to begin a social-health service revolution.

Objectives. The main aim is to build knowledge on the FCHN figure in the Italian context. To do that, the purpose is to first provide an accurate description of the state of the art regarding the FCHN national implementation through a mixed-method multicenter study. The specific endpoints will be to identify the current presence of this figure within our health system, and to gather information on their work and their feeling on their professional identity. Secondly, a systematic literature review will be done to identify the FCHN sensitive outcomes in an international viewpoint. By this study it will be possible also to gain information regarding the type of interventions performed by the FCHN and the type of measures administered during the family and/or community assessment. Finally, an evaluation of the impact of the FCHN on a defined number of families will be carried out.

Expected results. To highlight the role of FCHN in the family and community setting; to identify the state of the art of Italian FCHN; to define FCHN sensitive outcome, interventions and measures of assessment; to test the efficacy of the FCHN in the Italian context. The FCHN could really represent a public health key figure, acting as a coordinator of the care process in primary care setting. Giving the point of where the FCHN are in our nation and building a systematic knowledge on this figure and his capabilities could be the turning point for a social-health service revolution.

COVID-19 HEALTH EMERGENCY: CENTRAL ROLE OF THE E-LEARNING COURSE OF THE ISTITUTO SUPERIORE DI SANITÀ FOR HEALTH PROFESSIONAL PREPAREDNESS AND RESPONSE

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Background. On January 31, 2020, Italy declared a public health emergency concerning the novel Coronavirus Disease named COVID-19 by the World Health Organization. On February 28, 2020, the Istituto Superiore di Sanità (ISS) promptly launched the first e-learning course to train healthcare professionals entitled “Health Emergency from the Novel Coronavirus SARS-CoV-2: Preparedness and Response”.

Objectives. In this research study, we investigate: 1- Methods and technology of the first e-learning course available on the EDUISS platform in response to the COVID-19 pandemic (<https://www.eduiss.it>); 2- Efficacy of the e-learning course including completion rate and dropouts, numbers and types of enrolled healthcare professionals; 3- Evaluation of knowledge acquired by participants, their level of satisfaction and course’s quality; 4- Effectiveness of technological infrastructure and participants’ skills using EDUISS.

Preliminary Results. Between February 28 and April 28 2020, the ISS launched the first distance course to train Italian healthcare professionals in response to the COVID-19 outbreak. The course included three training units for a total of 16 hours based on the Problem-Based Learning (PBL) teaching method and was free of charge. During the delivering, the course significantly exceeded the projected participation rate. The number of participants was more than doubled, totaling 215,000 participants. Preliminary data analyses show that about 70% participants successfully completed the course, improved their professional knowledge with high satisfaction for course contents, methodology and technology.

Future perspectives. Since 2004, ISS has been delivering distance training for Public Health by EDUISS platform integrating active methodologies such as PBL with e-learning tools provided by Learning Management System Moodle and recently, Totara Learn. During the national emergency, the EDUISS platform promptly played a central role in the education and training of Italian healthcare professionals becoming a fundamental learning tool after March 2020, when no attendance courses could be held. Considering the clinical and management implication of this pandemic, it is also fundamental to conduct a training needs assessment among the Italian healthcare professionals to identify any gaps or areas to further improve e-learning courses and to support the scientific community in particular during health emergencies.

GENDER AND HEALTH IN ITALIAN JAIL: PREVALENCE OF HUMAN PAPILOMAVIRUS (HPV) INFECTION, PREVENTION AND TREATMENT STRATEGIES. A PILOT STUDY

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Background. The Legislative Decree of October 2, 2018 n°123 aims to strengthen assistance within prisons and to ensure to prisoners timely services, medical examination of the prisoner upon entering the institution and continuity of ongoing health treatments. Data from Italian penitentiary institutions indicate the presence of at least one pathology in 60-80% of prisoners, the pathology is an infectious disease in almost half of these cases (48%). Human Papillomavirus (HPV) infection is one of the most common sexually transmitted disease. The majority of infections are transient and asymptomatic. However, if the infection persists, it could manifest itself with a variety of lesions on the skin and mucous membranes, in relation to the type of HPV involved (high/low risk). It was demonstrated that women with detention experience have higher risk factors (high tobacco use rates, sexually transmitted infections, engagement in sex trade, etc.) than other women, this kind of factors are strongly linked to the risk of developing cervical cancer. The risk is four or five times higher compared to that found in women not in prison. However, very little is known about the burden of HPV infection in the population with a history of male criminal justice. The current rate of execution of screening tests for gynecological pathology is not known, nor the rate of execution of vaccination for HPV in subjects which it would be recommended to (both men and women). The limited availability of information in literature on the knowledge and experience of HPV vaccination by prisoners could lead to an increase in the disparity in the prevalence of HPV related diseases compared to the general population.

Objectives. The aim of the study is to obtain data on the prevalence of HPV infections on female people in detention in pilot penitentiaries and to study any gender and social differences, comparing the data emerged in the female prison population with those of the male prison population and with respect to the general female population.

Expected results. The study will allow to deepen the knowledge of a population with specific characteristics and to investigate the possible gender-specific differences of people in detention.

Future perspectives. In addition to the challenges that are faced daily in a prison context, there are opportunities to make an early diagnosis and manage infectious diseases, such as HPV. By analyzing the results, it will be possible to develop gender-specific strategies aimed at improving the health of the prison population.

ROLE OF ESTROGENS AND THEIR RECEPTORS IN THE DEVELOPMENT OF SKIN TEARS EVALUATED IN RESIDENTS OF RESIDENTIAL CARE FACILITIES

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Background. Skin Tears (ST) or "laceration injuries" or "flap wounds" are injuries that are often found in residents of Residential Care Facilities (RCFs). STs were first defined by Payne and Martin in 1993 as traumatic wounds, located mainly in the upper limbs, caused by "shearing", friction or mechanisms combined with the consequent separation of layers of skin. Skin Tears can cause psychological problems for the patient and represent an economic problem with important repercussions on both the patient and the community. The etiology suggests that the physiological changes of the skin related to old age, together with comorbidity, are among the main risk factors for their onset. The precise data on the phenomenon are not many, but it is estimated that STs are much more frequent than the same pressure ulcers, observing prevalence rates in RCFs around 40%. Therefore, there are several risk factors hypothesized so far. Much evidence has correlated, in various physiological or pathological conditions, the role of estrogens with the functions and aging of the skin.

Objectives. The project will develop on the analysis of populations of residents from RCFs belonging to the national territory. Two populations of residents cared in the RCF will be recruited. A group of subjects suffering from skin tears (group A) and a control group of subjects without skin tears (group B). The inclusion of patients in both groups will take place through a simple randomization procedure. Group A patients will be staged according to the STAR classification for skin tears. For each group a peripheral venous blood sample will be taken (to measure the levels of estrone and estradiol) and a skin biopsy will be performed in order to measure Estrogen Receptors (ERs) expression. A data collection sheet with anagraphic and anamnestic data will be developed to correlate the demographic and comorbidity data with the clinical conditions of the patients and with the laboratory findings from the sampling.

Expected results. The primary endpoint will be the correlation between serum estrogen levels, receptor expression and the presence of skin tears. The secondary endpoint will be Correlation between receptor structure and clinical staging of skin tears.

Future prospectives. We believe that our study may open new frontiers in the prevention and in the management of these skin lesions.

ENVIRONMENTAL ENDURANCE OF THE BETACORONAVIRUS SARS-COV-2

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Background. The COVID-19 disease, a respiratory disease transmitted by a new beta coronavirus SARS-CoV-2. As for other viral respiratory agents, SARS-CoV-2 spreads by person to person through respiratory droplets and direct contact and potentially by indirect contact through fomites. The goal of the current project is to evaluate whether the increase of temperature can influence the environmental endurance of SARS-CoV-2.

Objectives. Study of temperature influence on virus stability evaluate that viral spread could be influenced by climatic conditions since enveloped viruses tend to reduce their circulation in summertime owing to high temperature and solar radiation. The current spread of COVID-19 along the equator and tropics has been significantly less. In Italy, phase two of the emergency is close to the summer, and the increase of temperature may reduce COVID-19 prevalence. In order to try to predict the effect on the epidemic dynamic of COVID-19 in high temperature this project aimed to test SARS-CoV-2 environmental stability in parallel at room temperature (RT, 20°C-25°C) and at average maximum temperature estimated at 28°C in Italy.

Expected results. Statistical analysis of data could be able to shows that the virus vitality on plastic surface rapidly declined by more than 1 log₁₀ in TCID₅₀ during the first 24-36 hours, at RT. This trend could be confirmed by titration by plaque assay. At higher temperatures the same decay may observed more rapidly, indicating that viral infectivity can be influenced by higher temperature. A remarkable difference between the two temperatures could suggest that virus vitality can be influenced by the environmental temperature.

Future perspectives. The results of this study can support the hypothesis that in the hot season the increase of temperature may influence the environmental endurance of the SARS-CoV-2 and reduce COVID-19 transmission probability. Accordingly, we can assume that the higher temperatures might help decline of the number of infected people limiting the risk of new outbreaks of COVID-19.

NEW ENTOMOLOGICAL SAMPLING METHOD FOR THE SURVEILLANCE OF VECTOR-BORNE PATHOGENS

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Background. Vector-borne diseases account for more than 17% of all infectious diseases, causing more than 1 million deaths annually. Global travel, trade and environmental challenges can affect their transmission, causing the introduction or re-introduction of pathogens in countries where they were unknown or eradicated. Early detection of pathogens in arthropod vectors is highly important in prevention of vector-borne diseases and has the potential of providing the timely indicator of pathogens circulation before reaching humans.

Objectives. The aim of this study is to develop a new entomological surveillance approach that can be used in different contexts both of endemic and emerging vector borne diseases areas. For this purpose, we propose a trapping system able to i) detect directly the pathogen circulating in a specific area and preserve pathogen RNA/DNA in samples collected without the need of cooling chain ii) work in autonomy without frequent servicing thus reduce the economic and working effort, an essential feature in remote areas useful also in other contexts.

Preliminary results. We have modified a trapping device for mosquito monitoring (BG Sentinel) in which pathogen nucleic acids carried by infected specimens can be preserved for several days at environmental temperature and subsequently molecularly detected. The trap is provided with an artificial feeding system, based on the assumption that it is possible detect pathogens in mosquito saliva released during a sugar meal directly on FTA card soaked with a honey-based solution. We have tested the feeding system in laboratory and successively in the field in an Italian endemic area for West Nile Virus (WNV) in order to evaluate i) the best sugar solution and the feeding rate in mosquitoes ii) the modified BG trap's efficiency compared with CDC-CO₂ trap, commonly used as gold standard in WNV surveillance iii) the mosquito ability to release WNV on the feeder's card in field conditions iv) the possibility to molecularly detect the virus from the FTA card. Preliminary results confirm the ability of mosquitoes to take a meal on FTA cards, baited with a mixture of honey, hydroxyl-ethyl-cellulose hydrogel and methylene blue, both in laboratory and field conditions. Also, WNV is detectable in the cards from traps with infected mosquitoes, confirming a sufficient sensitivity of the system for surveillance purposes.

Future perspectives. The next step is to validate the system in tropical areas with circulation of different vectors and pathogens, such as Burkina Faso, a sub-Saharan country endemic for malaria.

MICROBIAL TRANSLOCATION AND INTESTINAL DAMAGE DURING SARS-COV-2, CLOSTRIDIUM DIFFICILE AND KLEBSIELLA PNEUMONIAE INFECTIONS: IMPLICATION FOR PATHOGENESIS

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Background. The main causes of infection in hospitalized patients are Clostridioides Difficile Infections (CDI) and intestinal colonization by Carbapenem-resistant Klebsiella Pneumoniae (KPC), which promotes subsequent KPC infection, rendering the intestinal involvement a common link between these two conditions. It has been observed that not only in bacterial but also in viral infections, there may be an involvement of the intestinal epithelium, a condition that might be a consequence of virus-host interaction. The recent pandemic due to SARS-CoV-2, a condition which has been recognized to have a systemic character instead of only a respiratory pattern, gained our attention, since the ACE-2 receptor, to which the virus binds to enter the cells, is highly expressed on Intestinal Epithelial Cells (IECs). Therefore, the common condition underlying SARS-CoV-2, CDI and KPC infection might be an alteration of intestinal mucosa and damage to IECs. As a consequence of mucosal perturbation, an increase in intestinal permeability might be observed during the course of these infections, a condition that might favour the translocation of bacteria or their products from the intestine to the extraintestinal space and systemic circulation, called Microbial Translocation (MT). It could therefore be possible that the degree of MT and Intestinal Damage (ID) might influence the clinical course.

Objectives. The main objective of this research is to evaluate the degree of alteration and damage of the intestinal mucosa during SARS-CoV-2, CDI and in patients with gut colonization by KPC and to correlate MT and ID with clinical outcomes.

Methods. For each subject with CDI, colonization due to KPC or with SARS CoV-2 infection, EndoCabIgM, antibodies neutralizing the LPS (Lypopolisaccaride) endotoxin core antigen, which are low in the case of MT; LBP, LPS binding protein, which is high in the case of MT; FABP-2, fatty acid binding protein 2, which is present in the circulation only after intestinal damage and IL-6, a marker of inflammation will be evaluated by ELISA assays. Expected results. We expect to demonstrate that MT, ID and inflammation may occur during SARS-CoV-2, CDI and KPC, therefore highlighting as the gut possesses a pivotal role in the pathogenesis of these conditions. In addition, we would correlate the extent of MT, ID and inflammation with the clinical outcomes.

Future perspectives. Assessing the presence and the degree of intestinal mucosal alteration could open the path to early detection of subjects with SARS-CoV-2, CDI and KPC colonization at risk of worse outcomes.

THE ROLE OF BIG DATA IN PUBLIC HEALTH, FROM THEORETICAL MODEL TO PRACTICAL APPLICATION

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Background. Since the past few years, there has been a growing interest for the use of massive amounts of data - i.e. the Big Data - in medical research, for their potential role in epidemiological research, in the analysis of the health needs, in prevention, treatment and management of medical conditions and in the development of healthcare policies. However, the analysis of such a huge amount of data poses significant challenges in obtaining evidence-based information. Another topic strongly linked with Big Data is the use of electronic instruments to monitor the person vital signs and the environmental conditions. Nevertheless, the technological advancement, combined with the ongoing demographic changes and the growing population expectations, can lead to economic imbalances in the management of the National Health System (NHS) and therefore it is necessary to carefully evaluate these new tools, in order to maintain the sustainability of the healthcare systems.

Objectives. The aim of the project is to address some of the emerging issues in the use of Big Data and electronic devices in medical research. It will focus on two aspects: 1) the ways in which Big Data can be effectively used in a public health perspective; 2) the use of electronic instruments and Big Data in the management of the chronic patients. Specific objective 1: To identify the methods of collection, analysis and use of Big Data in Public Health, an analysis of the methodologies and technologies currently available will be carried out to identify the most rigorous approach to obtain scientific evidence from these data. Specific objective 2: The results of the systematic review will be applied to a randomized clinical trial carried out on chronic patients assisted at the *Policlinico Umberto I*, that is already underway.

Expected results. At the end of the three-year period, the project activities will provide concrete know-how on the possibilities of Big Data and remote monitoring tools in public health, allowing their future application, highlighting the best method to be used for their analysis. At present, the search string for specific object 1 has been built and the retrieved articles are being evaluated.

Future perspectives. The practical application of these methods to a health management problem will allow the development of new and personalized supportive interventions for the management of chronic diseases, a fundamental field for the future sustainability of the NHS.

USE OF E-LEARNING MODULES TO PROMOTE PHYSICAL ACTIVITY AND WELLNESS AMONG NURSES IN ORDER TO IMPROVE MENTAL AND PHYSICAL HEALTH: A RESEARCH PROTOCOL

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Background. Maintaining a healthy lifestyle is an everyday challenge faced by the general population. Nurses are one of the health care professionals who are typically well-educated in taking care of the patients. There are studies that show that night shifts, extended shifts, and obesity has a correlation with the prevalence of acute low back pain among female nurses. Physical activity is the key factor in the prevention and treatment of many chronic diseases resulting in the improvement of quality of life. The impact of social media and technology on our lives is undeniable in the modern era. Establishing an online program with some qualities such as high level of convenience in access and use, summarized and to the point content, availability on social media, etc., can minimize the difficulties faced before and enhances the health of many nurses in healthcare institutions.

Objectives. The objectives of this study are to conduct a pilot study of five E-learning modules in order to determine their efficacy in improving mental and physical health among registered nurses in Rome, Italy, and to promote an active lifestyle among these nurses.

Expected results. I. Primary outcome - Mental health improvement, Physical health improvement; II. Secondary outcome - Knowledge on wellness, Body weight loss. At the end of this pilot study we expect an improvement in mood, emotional and physical health of nurses that participated in the exercise program. However, an improvement in physical activity level, fitness and awareness are expected among participants, they are expected to continue exercising all through their lifetime.

Future perspectives. Our study will enable the development and advancement of E-learning programs for promoting physical activity and wellness among nurses and health care workers in general.

THE USE OF REGENERATIVE MEDICINE TECHNIQUES IN PLASTIC SURGERY: ISSUES CONCERNING THEIR USE, LEGAL ASPECTS AND NEED OF GUIDELINES TO SHARE

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Background. Stem cell research is a very promising field in plastic surgery where the regenerative and angiogenetic properties of Adipose-Derived Stem Cells (ADSCs) are exploited to treat conditions characterized by sclero-atrophy (vulvar dystrophies, radiodermatitis, scleroderma, scarring) and for aesthetic purposes such as in the prevention and treatment of skin and vulvar aging.

Objectives. My aim is to evaluate the disputes, which may arise from regenerative medicine applications in the field of aesthetic and plastic surgery. Guidelines for the use of regenerative medicine therapies in plastic surgery are missing as are a statistically significant number of cases regarding disputes relating to their use. An analysis of these disputes will be undertaken in order to take into account issues concerning regenerative medicine clinical applications. Twenty Scleroderma patients with microcheily and microstomy will be enrolled. All of the patients will be treated with autologous fat transplantation in perioral region in order to obtain better mouth opening and an improvement in the patients' quality of life. Discontent relating to the treatment will be highlighted and evaluated. A review of literature will be performed together with an evaluation of randomized clinical trials and meta-analysis performing the quantitative analysis of the validity of results obtained with regenerative medicine techniques.

Expected results. On the basis of the encouraging results already obtained in tissue dystrophy, I expect patients to be satisfied with their aesthetic results. From the literature review, I will extract information regarding regenerative medical procedures, in order to draft explanatory documents on how to write an informed consent and how to perform the various techniques in a standard manner in accordance with the current legislation. This will form a solid base and guide practioners in the correct application of regenerative medicine procedures and highlight any critical issues.

Future perspectives. Based on the results obtained it will be possible to produce a list of the limits of products used in regenerative medicine and plastic surgery, in order to suggest adequate protocols for the management and control of these products in compliance with the current legislation. It will furthermore be possible to define appropriate, consolidated clinical indications for regenerative medicine applications, for which it is necessary that medical personnel are able to provide adequate care procedures. It will also be possible to provide a rigorous reference point, which could be shared with hospital and private practioners working in the fields of regenerative medicine and plastic surgery.

MODULATION OF HOST IMMUNITY TO MALARIA BY *SCHISTOSTOMA HAEMATOBIIUM*

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Background. In Sub-Saharan African populations, where *Plasmodium falciparum* malaria impose a high burden in terms of mortality and morbidity, *Schistosoma haematobium* is also highly prevalent. The geographical overlap in the distribution of these parasitic diseases and their high prevalence makes co-infections frequent. However, little is known about the immunological mechanisms involved in the co-infected host. A possible approach to the investigation of the impact of *S. haematobium* on immunity to *P. falciparum* is the comparison of populations showing different susceptibility to malaria.

Objectives. We aim to investigate the impact of infection with *S. haematobium* on immunity to *P. falciparum* malaria. Specific objectives are: i) characterize immunomodulatory molecules of *S. haematobium*; ii) measure the prevalence and intensity of *S. haematobium* infection among populations from Burkina Faso showing different immunity to *P. falciparum*; iii) identify humoral correlates of *S. haematobium* infection prevalence and intensity; iv) assess the impact of *S. haematobium* infection on immunity to *P. falciparum* infection among study populations; v) investigate the genetic basis of susceptibility to *S. haematobium* infection and identify loci affecting susceptibility to both schistosomiasis and malaria infection.

Expected results. We expect that the present research project combing *in vitro*, *in vivo* and epidemiological studies will provide novel insights into the ability of *S. haematobium* infection, through E/S products, to modulate the host immune response and thereby to affect immunity to malaria. Here I would summarise the preliminary results of the paper published in Acta Tropica.

Future perspectives. Our results will provide potential for application in products (drugs and vaccines) development and in malaria control.

IN VITRO CULTURE MODEL TO STUDY MERKEL CELL POLYOMAVIRUS MOLECULAR BIOLOGY AND ONCOGENIC MECHANISMS INVOLVED IN MALIGNANCIES OTHER THAN MERKEL CELL CARCINOMA

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Background. Merkel Cell Polyomavirus (MCPyV) is a small, double-stranded DNA virus, associated with a neuroendocrine, cutaneous malignancy, Merkel Cell Carcinoma (MCC). MCPyV has a circular genome bisected by a Non-Coding Regulatory Region (NCRR) into early and late coding regions. The NCRR contains the viral origin of replication, sufficient to initiate DNA replication, regulatory elements and bidirectional transcriptional promoters required for early and late viral gene expression. The early region includes the Tumor (T) antigen gene locus encoding for distinctive gene products: Large T (LT), small T (sT), 57kT and a product from an alternate frame of the LT open reading frame (ALTO). After the initiation of viral replication, the late region, encoding for the structural components of the virus capsid, Virus Protein 1 (VP1) and Viral Protein 2 (VP2), is transcribed from the opposite direction respect to the early region. The strong association of MCPyV in the development of MCC and the widespread of the virus across the body, incited researchers to investigate the role of MCPyV in *non-MCC*. It has been proposed that MCPyV may be associated with extra-pulmonary small cell carcinoma, cervical cancer, other types of skin cancer, lung cancer and even some types of leukaemia. However, many of the examples displaying the detection of the virus in the various non-MCC, are not able to clearly demonstrate a direct connection between cellular transformation and the presence of the virus.

Objectives. Since mechanistic studies to fully investigate MCPyV molecular biology and oncogenic mechanisms in malignancies, other than MCC, have been hampered by a lack of adequate cell culture model, the goal of this project will be to identify cell types or cell lines, different to fibroblasts from the dermis, that support MCPyV infection and replication with particular attention to determine the state of the viral genome (episomal or integrated) and to define the contribution of LT viral protein to transformation and cancer growth in non-MCC.

Expected results. Establish *in vitro* MCPyV systems to gain a better understanding of permissive cell lines that support MCPyV infection and in which MCPyV infection could lead to non-MCC development.

Future perspectives. Since several studies indicate that MCPyV sT may be the main oncogenic protein, the expression of sT, will be assessed. Moreover, since sT was recently detected to induce genomic instability in its host genome by targeting the E3 ubiquitin ligase, this hypothesis will be verified by experimental future studies.

CHARACTERIZATION OF THE MUCOSA-ASSOCIATED MICROBIOTA AND EVALUATION OF ITS IMPACT ON TPH1 AND SERT GENES EXPRESSION IN CIPO PATIENTS

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Background. The Chronic Intestinal Pseudo-Obstruction (CIPO) disease is a rare severe gut motility disorder characterized by symptoms of intestinal mechanical obstruction in absence of a real physical blockage. Clinicians don't have a unique effective diagnostic tool for CIPO patients, and the most advanced diagnostic tools and treatments available could only relieve patients' symptoms. This leads to a late diagnosis and an increased mortality rate for these patients. CIPO is linked to a Gastrointestinal (GI) motility slow-down and this motility is controlled by the Enteric Nervous System (ENS). In the ENS, neurons are interconnecting through neurotransmitters, counting dopamine, acetylcholine, and serotonin. Intestinal dilation and slow transit have been shown to contribute to intestinal bacterial growth (SIBO) and intestinal imbalance in patients with CIPO. Many are the evidences linking gut microbiota and intestinal motility disorders but, up today, no studies have certainly connected gut microbiota and its byproducts with motility disorders in CIPO patients. These investigations are essential to reveal microbiological marker species, bacterial consortium or bacterial metabolites having the main influence on intestinal motility, and the pathways involved.

Objectives. This project aims are i) to characterize the mucosal adherent bacteria of pediatric CIPO patients, in order to verify the existence of a specific microbiota that can be associated with this disease and ii) to evaluate the expression of the genes involved in the synthesis (TPH1) and reuptake of Serotonin (Sert), in order to understand whether variations in the expression of these genes could be influenced by the composition of the mucosa-associated microbiota, and vice versa, also verifying whether epigenetics factors (methylation levels and histone changes of their promoters) are involved. The bioptic samples, from colon and ileum of CIPO pediatric patients, are provided by the Sant'Andrea Hospital of Rome and the Cesare Arrigo Hospital of Alessandria.

Expected results. The study, through the characterization of microbial communities associated with the intestinal mucosa and the assessment of the impact of these communities on the expression and on the epigenetic profiles of the genes coding for the enzyme TPH1 and the serotonin-carrying protein SERT, will allow to better understand the mechanism by which the microbiota influences the intestinal peristalsis in CIPO patients.

Future perspectives. The results obtained could give the opportunity to develop alternative diagnostic approaches for CIPO patients. The highlighting of pathological and therapeutic microbial markers may also reveal new therapeutic possibilities, including targeted gut microbiota manipulation, which could improve these patients' conditions.

MOLECULAR CHARACTERIZATION AND PREVALENCE OF PROTOZOAN AND METAZOAN PARASITES INFECTING NON-HUMAN PRIMATES IN NATURAL AND CAPTIVE CONDITIONS

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Background. Non-Human Primates (NHP) have been found infected with diverse intestinal zoonotic protozoan and metazoan parasites of public health concern. *Blastocystis* subtypes have been reported in free ranging and captive NHP from the New and Old World. Furthermore, *Giardia duodenalis* assemblages A and B, and *Entamoeba* species have been reported in NHP. The occurrence of zoonotic helminths has also been observed in NHP, for instance, *Trichuris* spp. and *Ascaris* spp. Ecosystem transformation could increase the contact between humans and NHP, leading to implement zoonotic transmissions, likewise, captivity conditions can represent potential scenarios for occupational risks due to parasitic infections.

Objectives. This study aims to explore the prevalence and genetic diversity of intestinal parasites from NHP living in fragmented forests in Colombia, in a preserved forest in Ecuador, and in a wildlife recovery centre in Italy, in order to explore zoonoses and correlation with the transmission pathways. The objectives are 1) to molecularly characterize protozoans (*Giardia* spp., *Blastocystis* spp., *Entamoeba* spp.) and helminths (*Trichuris* spp., *Ascaris* spp.) in NHP, 2) to determine parasite prevalence, and 3) to estimate genetic diversity, in order to assess zoonotic potential.

Expected results. It is expected to find differences in the prevalence of parasites in NHP living in the preserved forest in comparison with NHP living in the recovery centre and the fragmented forests, as exposure may vary depending on the circulation of parasites. Additionally, we expect to successfully characterize the assemblages/species/subtypes of parasites circulating in each environmental condition.

Future perspectives. The results of this study could be useful within NHP conservation programs, as well as in public health policies.

AMBULANCE SANIFICATION: AN HYGIENIC, LEGAL AND OCCUPATIONAL MEDICAL CHALLENGE

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Background. Usually, the interior of ambulances and the non-consumable items do not undergo sanification between two consecutive interventions. Sanification is normally performed once or twice a day. This allows passage of micro-organisms from a patient to the next, and it may cause the emergence of multi-resistant pathogens and the insurgence of related diseases. On the other hand, health personnel is known to use (and abuse) products for skin sanification, especially alcohol based ones. It has been demonstrated that such usage is not only harmful for skin bio-film, but is also responsible of microscopic lesions on the skin itself, that may allow pathogen infection.; also, ingestion and inhalation of such substances for long period of time, despite low dosage, may cause insurgence of occupational diseases.

Objectives. To analyze, in a quali-quantitative manner, micro-organisms present in the interior of ambulances used for emergency transport of patients in the Rome province, and eventual related diseases found in the transported patients. Qualitative analysis of substances inhaled by health personnel within the same ambulance. Analysis of economic and social costs from such diseases.

Expected results. As international literature also reports, a variable quota of ambulance-transported patients developes pathologies related to pathogens that are found within the ambulance interior. Health personnel working on ambulances is more prone to develop respiratory illnesses than the static (i.e. hospital) counterpart. Such diseases have both direct and indirect costs for the health system.

Future perspectives. A widespread knowledge and usage about skin sanification products may reduce the risk of developing acute and chronic diseases, and allow to save the associated costs.

MOLECULAR BIOLOGY OF ASPHYXIA DEATHS: EXPRESSION PROFILES OF HYPOXAMI IN THE PULMONARY RESPONSE TO HYPOXIA

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Background. The forensic investigation of asphyxia deaths still poses a challenge due to the need to demonstrate vital exposure to hypoxic insult according to high levels of evidence. Over the years, constant research has been aimed at studying the molecular response to the decrease in oxygen tension. The effects of hypoxia in the lung are complex and an understanding of the mechanisms underlying the acute toxicity induced by hypoxia is still incomplete. The main objective of the study is to identify a miRNA panel whose expression at the lung level is induced by an acute hypoxic insult. At the same time, the comparison between the expression profiles of hypoxamiR and immunohistochemical markers of hypoxic stress on lung tissue will allow evaluating the sensitivity and specificity of the methods.

Objectives. The study population will consist of at least 20 cases of asphyxia and 20 cases of traumatic death. The main objective will be to evaluate the diagnostic potential of hypoxamiR in the diagnosis of asphyxia through the comparison with the immunohistochemical markers currently in use (anti-HIF-1 α and e-NOS). For this purpose, the quantitative analysis on the hypoxamiR of interest - selected from the literature - will be carried out through RT-PCR after extraction of all the RNAs. The expression profiles of miRNAs will finally be analyzed through the ROC curve and the Area Under the Curve (AUC).

Expected results. The evaluation of the expression profiles (downregulation and upregulation) of the selected miRNAs will provide interpretative elements useful for understanding the mechanisms involved in the pulmonary response to hypoxia. The concomitant immunohistochemical evaluation may provide confirmation of the protein expression modifications consequent to the acute decrease in the oxygen concentration.

Future perspectives. The results obtained will help to implement the diagnostic investigations available to the forensic pathologist in the evaluation of asphyxia deaths by integrating the current knowledge on the molecular biology of the lung response to hypoxia. Nonetheless, the proposed method will ensure the sustainability and reproducibility of the results by allowing the design of studies based on extraction from formalin-fixed and paraffin-embedded tissues, given the intrinsic stability of miRNAs in the various degradation processes.

THE ROLE OF TARGETED HIV SCREENING IN THE EMERGENCY DEPARTMENT

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Background. Human Immunodeficiency Virus (HIV) infection continues to expand worldwide and a significant proportion of infection is still undiagnosed. Recent studies have addressed the impact and feasibility of *opt-out* HIV screening in Emergency Departments (EDs) in urban settings at high HIV prevalence, whereas little is known about the yield of implementing *targeted* HIV testing especially in low-prevalence areas.

Objectives. The present study undertakes a scoping review of research carried out on the implementation of targeted HIV screening in adult EDs to determine the impact, feasibility and acceptability of HIV testing in different HIV prevalence settings.

Results. The search returned 416 articles. Of these, 12 met inclusion criteria and were included in the final review. Most of the included studies were carried out in the United States ($n=8$; 67%) and in areas of high HIV prevalence ($n=11$; 92%). Three (20%) were randomized control studies. While the rate of newly diagnosed HIV cases varied widely (0.03-2.2%), likely due to methodological heterogeneity between studies, the linkage to new HIV diagnosis was often high (80-100%) and median CD4+ cell count was always greater than 200 cells per microliter. Targeted HIV screening was found to be cost-effective and well accepted by participants.

Future perspectives. Targeted HIV screening at the ED can be impactful, feasible and well accepted, but often requires extra funding and staff. Most previous work has focused on areas of high disease prevalence. Studies addressing the role of targeted HIV testing in ED in low prevalence setting are warranted.

DREAM - DISABILITY IN REFUGEES AMONG MEDITERRANEAN

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Background. In 2018, 638 thousand asylum seekers applied for international protection in the Member States of the European Union (EU), down by 10 % compared with 2017. The reasons for this trend reversal are probably due firstly to recent international agreements between the EU and Turkey, then to the agreement between Italy and Libya that imposed the creation of detention camps to avoid migrants departure towards EU borders. Currents EU policies do not include the rights of migrants' people and certainly overlook the rights of migrants people with disabilities. Furthermore, the reception process in Italy and Greece, as well as the long detention of asylum seekers in other host states, does not alleviate health problems, but rather contributes to the aggravation of illness and trauma. There is limited evidence on the prevalence of disability amongst refugees and asylum seekers, with reported estimated disability rate varying from 3% to 10%. Different studies report physical health problem in 1/6 refugees and mental health problems in 2/3 refugees. There is no universal model to meet the rehabilitation needs of refugees, and priorities can vary greatly among population groups and contexts. A comprehensive evaluation of individual needs and their prioritization for rehabilitation should be undertaken (in the field), by qualified healthcare professionals.

Objectives. To assess disability among migrant population in a Global Health perspective.

Expected results. A community-based survey was conducted from July 2018 to January 2020 in Italy. People hosted in governmental first reception centers and in official temporary facilities were involved. Two different assessment tools were used: the Washington Group Extended Set on Functioning (WGES-F) and the Community-Based Rehabilitation Indicators. Data were analyzed as descriptive analysis. 40 people were involved in this interview. The majority came from the Horn of Africa and from West Africa. The WGES-F showed as main functional impairment the mental health (memory, anxiety, depression), followed by tiredness and pain. CBR Indicators highlight the needs of prevention actions and more involvement in health decision making. Furthermore, the total of people interviewed state to do not have enough money to satisfy their needs. More of them, despite is involved in vocational training, they believe that these have partially or none utility. More than half would like to be involved in self-help groups, but this service is not provided in reception centers.

Future perspectives. This survey lays the foundation to develop a well-structured program in a Community-Based Inclusive Development perspective. Actions should primarily focus on livelihood, social and empowerment domains. For health component, is recommended outreach for health professionals, in order to increase people involvement and respect.

DEVELOPMENT OF A PREDICTIVE ALGORITHM FOR LOSS EVENTUALITY ASSESSMENT IN LITIGATIONS CONCERNING MEDICAL LIABILITY

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Background. In healthcare institutions, clinical risk management includes a set of methods, tools and actions that allow risk assessment and treatment in order to improve patient safety, which was made part of the right to health by the Italian law 24/2017. Medical liability litigation is part of the clinical risk. To the best of our knowledge there are no standardized tools or objective references to quantify the probability of loss for Institutions deriving from a civil trial concerning medical liability.

Objectives. We intend to design an operational tool to attribute a definite probability of loss to each litigation before the judicial phase. We will implement a first phase of collection and organization of big data relating to past disputes of healthcare facilities in conjunction with Sapienza University to set up a single data warehouse. The second phase will consist in the design of a predictive function capable of deriving the result required by the variables available through the construction of a neural network. In this way the systematic retrospective review of known cases will provide the group of training examples for subsequent analysis.

Expected results. The aggregate analysis will proceed through a neural network synthesized as a set of decision trees. The final result will attribute the risk of loss, starting from the insertion of known parameters relating to the accident. The tool obtained will consist of dynamic software capable of automatic updating and correction based on the comparison between predicted results and new real events observed.

Future perspectives. The formulation of the risk of loss according to a continuous spectrum of probabilities could be applied as a scale of coefficients to the technical estimates commonly used to set aside funds from the corporate budget destined for compensation from civil liability. The same amounts, moreover, defined in an objective and standardized way can be used as actuarial references in the conciliation negotiations of the disputes outside the courts.

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