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XII Seminar - PhD Day

Happiness is a simple system

Virtual Meeting
Organized by the Italian National Institute of Health
and Sapienza University of Rome
Rome, July 15-16, 2021

ABSTRACT BOOK

Edited by
E. Renzi, I. Bernardini,
F.M. Damato and A. Di Pucchio

ISTITUTO SUPERIORE DI SANITÀ

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Edited by
Erika Renzi (a), Ilaria Bernardini (a, b),
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2021, xiii, 93 p. ISTISAN Congressi 21/C2

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Key words: Happiness; Simple/complex; Microbiology, Infectious diseases, Public health, Social medicine, Forensic medicine

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L'ultima Giornata dei Dottorandi di Malattie infettive, microbiologia e sanità pubblica è stata influenza e dominata dalla pandemia da COVID-19. L'evento di quest'anno prova a uscire da questa visione emergenziale, con relazioni a invito dedicate a due aspetti: la felicità e il contrasto tra semplicità e complessità. La felicità è intesa nel più ampio concetto di benessere, mentre la dicotomia semplice/complesso rappresenta un paradigma di sistemi biologici che richiedono sia complesse interazioni sia soluzioni adattative semplificate.

Parole chiave: Felicità, Semplice/complesso, Microbiologia, Malattie infettive, Sanità pubblica, Medicina sociale, Medicina legale

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Claudio Bandi	Department of Biosciences, University of Milan, Milan, Italy
Guido Caldarelli	Department of Molecular Sciences and Nanosystems, University Ca' Foscari, Venice, Italy
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Paolo Villari, Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy
Stefano D'Amelio, Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

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Stefano D'Amelio, Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

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PREFACE

The PhD Day represents a traditional, successful event in the activities of the PhD in Infectious diseases, microbiology and public health. The last meeting of PhD students in Infectious Diseases, Microbiology and Health has been strongly influenced by, and focused on the COVID-19 pandemic. The XII meeting tries to get out from the emergency, with invited talks dedicated to two aspects: happiness and simplicity/complexity. Happiness is intended as the including the comprehensive concept of well-being, while the contrasting simple/complex dichotomy is a paradigm of biological systems that requires both complex interactions and simple adaptive solutions.

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

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The Scientific Staff
Ilaria Bellini, Ilaria Bernardini, Arianna Di Rocco,
Erika Renzi, Marco Tofani, Valentina Perri,
Silvia Venturini, Livia Besi, Felice Marco Damato,
Nicola Di Fazio, Alessandra Di Pucchio

PhD candidates' communications

PREVALENCE OF MUSCULOSKELETAL DISORDERS IN A LARGE SAMPLE OF ITALIAN WORKERS: OCCUPATIONAL AND HEALTH-RELATED RISK FACTORS

Giovanna Adamo (a), Sergio Iavicoli (b), Paolo Villari (a)
(a) Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy
(b) Italian Workers' Compensation Authority (INAIL), Department of Occupational and Environmental Medicine, Epidemiology and Hygiene, Monte Porzio Catone, Rome, Italy

Background: Work-related Musculoskeletal Disorders (WMSDs) represent an important socio-economic burden. The currentwesx risk assessment and management involved in the ethiopathogenesis of WMSDs is based on observational tools and checklists, which have some limitations in terms of accuracy and reliability. The aim of this study was to assess WMSD prevalence and identify possible correlations with several socio-demographic and work-related variables in a large cohort representative of Italian workers in order to improve our understanding of the WMSD phenomenon.

Methods: This study includes data from INSuLa, a cross-sectional nationally representative survey of health and safety at work, developed by the Italian Workers' Compensation Authority. A total of 8,000 Italian workers were included. Multivariate logistic regression analyses were performed to evaluate the association of independent variables, such as workers' perceptions of exposure to biomechanical/ergonomic and Video Display Unit (VDU) risks (Risk Perceived) and the actual risk exposure (Risk Detected) on Back, Lower and Upper limb pain. Socio-demographic, occupational and other health-related variables were included to investigate possible association with musculoskeletal disorders.

Results: The probability of experiencing WMSDs increases with age and is higher among women, workers with lower educational level and overweight/obese workers. Workers reporting higher level of work-related stress and insomnia had significantly higher odds of experiencing all three WMSDs. In addition, depression was found to be significantly associated with Lower limb and Shoulders, neck and/or upper limb pain. Other interesting findings are those related to the risk perception compared to risk detection linked to WMSDs. Specifically, workers perceiving a significant exposure to biomechanical/ergonomic risk but not included in a health surveillance program for such risk (Risk Perceived/No Risk Detected) had significantly higher odds of reporting musculoskeletal disorders. Such workers were mainly in the 19-24 age range (39.9%), transportation, warehousing/information and communication sectors (38.9%) and employed in companies with more than 250 workers (35.8%).

Conclusions: Our findings confirm that WMSDs are extremely important and currently represent a stimulating and complex health challenge for both occupational medicine and public health professionals. Further studies aiming at improving our understanding of emerging risks for WMSDs, identifying gaps in current evaluation strategies and informing preventive workplace interventions are needed.

INTESTINAL PERMEABILITY AND MICROBIAL TRANSLOCATION DURING CORONAVIRUS DISEASE-19

Dania Al Ismail, Maria Claudia Miele, Federica Di Timoteo, Massimiliano De Angelis, Vera Mauro, Raissa Aronica, Giancarlo Ceccarelli, Claudia Pinacchio, Gabriella D'Ettorre, Mariateresa Mascellino, Claudio Mario Mastroianni, Alessandra Oliva
Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

Background: Intestinal involvement has been described during Coronavirus Disease-19 (COVID-19), with up to one-third of COVID-19 patients also experiencing gastrointestinal symptoms such as diarrhea and vomiting along with the most common respiratory symptoms. However, biomarkers of Microbial Translocation (MT) and Intestinal Damage (ID) are still poorly explored in COVID-19. The main purposes of this project were to assess i) whether an alteration of gut permeability and cell integrity is present during the course of COVID-19 and, ii) if present, whether the degree of this alteration is more pronounced in severe infection.

Methods: Over a period of 6 months (March 2020-July 2020), patients with COVID-19 hospitalized at Sapienza University (Rome) were enrolled in the study. For each subject, blood samples were collected at COVID-19 diagnosis (T0) and after 7 days (T7), respectively. Patients were further divided into those requiring Intensive Care (ICU) admission or not. Markers of MT [LPB (Lipopolysacharide Binding Protein) and EndoCab IgM] and ID [I-FABP (Intestinal Fatty Acid Binding Protein)] were evaluated using enzyme-linked immunosorbent assays (ELISA) in plasma. As control group, non-hospitalized healthy donors (HDs, n=16) matched for age and sex with negative SARS-CoV-2 RNA detection were enrolled.

Results: A total of 45 patients with COVID-19 were included in the study, median age 66 (56-71) years, 27 males and 18 females. Median duration of symptoms before COVID-19 diagnosis was 3.7 (2.7-9.7) days. Among symptoms, gastrointestinal involvement was observed in 4 subjects (8.8%). Twenty-one patients (46.6%) were admitted to ICU and overall mortality was 22% (10/45). Compared to HD, a high degree of MT and ID was observed during COVID-19, which was maintained, if not increased, from T0 to T7. Similarly, patients who were admitted to ICU had higher levels of MT but not of ID than patients not admitted to ICU. At univariate analysis, high levels of LBP were associated with mortality (p=0.04), whereas at multivariable analysis only the occurrence of thrombotic event was independently associated with death (p=0.018).

Conclusions: Patients with Coronavirus Disease-19 exhibited high level of MT, especially in subjects with more severe infection. COVID-19 is associated with gut permeability and alteration of intestinal mucosa.

PRACTICAL IMPLEMENTATION OF ONE HEALTH IN VECTOR-BORNE AND EMERGING DISEASES

Laura Amato (a), Francesca Cito (a), Maria Grazia Dente (b), Silvia Declich (b), Paolo Calistri (a)

(a) National Reference Center for Veterinary Epidemiology, Istituto Zooprofilattico Sperimentale dell'Abruzzo e del Molise "G. Caporale", IZSAM, Teramo, Italy

(b) National Centre for Global Health, Italian National Institute of Health, Rome, Italy

Background: One Health (OH) concept became widespread in early 2000s as a theory in which animal health, human health and environment health are linked together. Despite its several possible applications, its use into practice still struggles, colliding with the old silos thinking.

Methods: Hereby, we describe the outcomes of the application of OH concept, highlighting pros and cons, in two different contexts: 1) MediLabSecure (DEVCO: IFS/2018/402-247), a networking project focusing on early warning integrated strategies against arboviruses; 2) the COVID-19 pandemic, which posed new challenges for Istituto Zooprofilattico Sperimentale dell'Abruzzo e del Molise (IZSAM), a Veterinary Public Health Institute.

Results: After a year and a half of activities, COVID-19 forced a stop in some networking events of MediLabSecure, but the partners showed an immense flexibility in divert the activities: the system provided support to beneficiary countries in different aspects of the management of the pandemic, from diagnosis to health personnel training. On the other hand, IZSAM was put into the frontline in COVID-19 routine official diagnosis of human cases. This was the opportunity to consolidate connections with the Public Health Authorities, which lead to the development of research activities in human and animal sectors, to epidemiological studies and on-site surveys, and to the improvement of tools and dashboards for data visualization.

Discussion: In our study cases, OH not only was implemented successfully, but provided the strong background needed to face new challenges, as the COVID-19 crisis. The pandemic pushed for cross-sectorial collaborations, demonstrating its importance and potential, therefore outlining the way forward.

A NATIONAL SURVEY ON GLOBAL HEALTH EDUCATION

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(a) Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy
(b) Caritas Medical Area, Rome, Italy

Backgrounds: Global Health Education (GHE) in Italy has spread since the first decade of 21st century. The presence of Global Health (GH) courses in Italy was monitored from 2007 to 2013. In 2019, a new survey was proposed to assess the availability of educational opportunities in Italian medical schools.

Methods: An online survey was carried out using a questionnaire administered to a network of interested individuals with different roles in the academic world. It was sent with a presentation letter to students, professors, and members of the Italian Network for Global Health Education. The survey was also distributed through the National Permanent Conference of the Presidents of Academic Degree Courses in Medicine. The features of courses were analysed through an evaluation grid associated with a scoring system.

Results: A total of 61 responses were received from affiliates of 33 out of the 44 medical schools in Italy. The national mean of GH courses for each faculty was 1.2, reflecting an increase from 2007. The courses increased nationwide, resulting in a dispersed GHE presence in northern, central and southern Italy. One of the most critical points was related to the nature of "elective" courses, which were not mandatory in the curricula. Enrollees tended to be students genuinely interested in GH issues. Some community and service-learning experiences, referred to as GH gyms, were also detected at national and international levels.

Discussion: GHE has spreading in Italy in line with the vision of the Italian Network for Global Health Education. Although progress has been made to disperse GH courses around the country, more academic commitment is needed to include GH in the mandatory curricula of medical schools and other health faculties. The authors recognise the importance of GHE and propose to insert the main themes related with GH (social determinants of health, inequities in health, health systems, globalization and health, migration and health, international health cooperation) in the mandatory curricula of medical schools. The relevance of GHE is clearer than ever, especially considering the challenges related to the COVID-19 pandemic, during which inequities in health between different populations are once again evident and demonstrated. The authors hope that this survey, together with other articles which are already published or which forthcoming, could give an important contribution to the debate on GHE in Italy.

GENOTYPIC AND PHENOTYPIC FEATURES OF *S. AUREUS* INVOLVED IN ATOPIC DERMATITIS

Antonietta Lucia Conte, Maria Pia Conte
Department of Public Health and Infectious Disease, Sapienza University of Rome, Rome, Italy

Background: It is known that Skin Microbiota (SM) cooperates with skin immune system and protects against pathogens, representing an important factor for skin health. Different skin disorders, as Atopic Dermatitis (AD) a chronic inflammatory disease, have been linked to dysbiosis of SM. The pathogenesis of AD involves an increase of *Staphylococcus aureus* colonization. Moreover, it is documented that some *S. aureus* strains produce several virulence factors, colonize skin via biofilm and invade keratinocytes, thus contributing to increase inflammation. The aim of this study is to deepen the genotypic and phenotypic characteristics of *S. aureus* involved in AD.

Methods: A total of 15 AD patients were enrolled. For each patient, swabs from nose, lesional and nonlesional skin at flare (T0) and from nose and skin at post flare (T1) were collected. A total of 73 *S. aureus* isolates, 55 from AD patients and 18 from healthy carriers, were genetically characterized by RAPD-PCR. Biofilm production by *S. aureus* strains was determined through crystal violet staining. Invasion assays on human keratinocytes (HaCat cells) were also performed.

Results: At T0, *S. aureus* was recovered in 100% of lesional skin samples with a high degree of colonization (104-105cfu/ml); at T1 *S. aureus* was recovered in 50% of skin samples with a lower degree of colonization (102-103 cfu/ml). Furthermore, in 11/15 (73%) of the patients, at T0, *S. aureus* from the nose and the skin of the same patient belonged to the same clonal group. Differently, at T1, in 8/14 (57%) of the patients, *S. aureus* from the nose were genetically identical to those recovered at T0, while in 6/14 (43%) of the patients the skin isolates belonged to a different clonal group. Of 24 not clonal *S. aureus* strains, 58% were strong and 42% moderate biofilm producers. Furthermore, at T1 a higher percentage of invasive *S. aureus* strains (67% *vs* 22%) were detected.

Conclusion: These data confirm that *S. aureus* is the key pathogen of AD and that the high rate of its colonization correlates to disease severity. Overall, the high biofilm production could be functional to survival of *S. aureus* in this hostile environment, whereas the higher invasiveness observed in post flare could be important for its persistence. Currently, to deepen genomic features associated with pathogenic mechanisms, the analysis of the complete genome sequence of selected *S. aureus* strains is in progress.

THE QUANTITATIVE RELATIONSHIP BETWEEN RORSCHACH AND WAIS-IV: PATTERN DIFFERENCES IN IQ PROFILES

Felice Marco Damato, Serafino Ricci
Department of Anatomical, Histological Medical Legal and Locomotive System Sciences, Sapienza University of Rome, Rome, Italy

Background: Wechsler Adult Intelligence Scale-IV (WAIS-IV) and Rorschach Inkblot Test are often included in diagnostic routines by most of the clinicians to measure the "Performance" from two different points of view; while WAIS-IV is used to analyse intelligence and cognitive abilities, Rorschach measures how a subject respond, both emotively and cognitively, to unstructured stimuli.

Methods: The full study sample (N=34) was sorted into three groups based on the IQ score obtained by the WAIS test. Groups were composed in the following way: IQ lower than 69 (N=19); IQ ranging from 70 to 99 (N=6); IQ higher than 100(N=9).

Statistical analysis: To analyse differences between groups we used a univariate analysis of variance (ANOVA). In addiction differences between groups were deeply analysed using Bonferroni Post-hoc Test.

Results: The ANOVA analysis shows that moderate differences exist between the groups for the parameters Zd, Zsum, S, M, Zf, R (p=0.05). On the other hand, strongly significant differences were found on the following parameters WSC, Complexity, Human responses, Animal detail, unusual form quality, W (p=0.01).

Discussion: The results show how the analyses carried out provide statistically significant characteristics to detect a prototypical profile of a subject with a diagnosis of intellectual disability. Considering also legal and social medicine aspects, the identification of these patterns represents a substantial help for clinicians to recognize the "state of handicap" useful to access to the benefits provided by Italian welfare state and especially by law 104/92.

REVIEW ABOUT APPLICATION OF LAW 24/2017 (GELLI) DURING THE FIRST FOUR YEARS SINCE ITS ENTRY IN FORCE AND NEW APPLICATION FOR PANDEMIC COVID-19 FROM FEBRUARY 2020

Umberto De Gennaro, Vittorio Fineschi, Raffaele La Russa
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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' 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. Italy was the first western country to deal with a totally new health emergency, never faced until February 2020, when the first autochthonous case was registered. It was no easy for anyone, but above it was not easy for the health personnel who fought, daily and relentlessly to guarantee each individual the sacred right to health despite the difficulties. Precisely from the questions and the continuous news that accompanied our days, the need arises to deepen the scope of this emergency, top understand the instrumentals in possession of international law and Italian law, to try to outline complete picture of the medical responsibilities, but above all to analyse an extremely vast and varied area, the relevance of which appears more and more current every day.

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 5-813-15. 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. Review for cases of professional responsibility by Pandemic COVID-19 during 2020-2021.

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

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

Expected results: PMCT 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, etc.) that are able of causing traumatic death].

EPIDEMIOLOGY AND CLINICAL IMPACT OF AIRWAYS COLONISATION FROM *FILAMENTOUS FUNGI* IN ADULT PATIENTS WITH CYSTIC FIBROSIS

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Background: Isolation of *Filamentous Fungi* (FF) in Cystic Fibrosis (CF) has been increasingly reported over the past decade. However, their real prevalence is hard to estimate due to different sputum processing protocols across laboratories. Primary aim of the present project was to assess the prevalence of airways colonisation from *Aspergillus spp*. and *Non-Aspergillus Filamentous Fungi* (NAFF) in a large UK cohort of adult CF patients obtained by the adoption of standardised extended fungal cultures (EC - i.e., 4 weeks) compared to routine laboratory cultures. Secondly, we aimed to assess the effects of colonisation from FF on the most important clinical outcomes in CF.

Methods: A retrospective analysis of data collected from the adult CF Centre of the Royal Brompton and Harefield NHS Foundation Trust (London, UK) local patient registry was performed. Microbiological data were collected annually from sputum cultures performed between 2010 to 2019. Patients were considered colonised if they had ≥1 positive sputum culture over each year. Comparison was made between data from two 5-year periods: 2010-14 (T1) *vs* 2015-19 (T2) - i.e., before and after EC processing was introduced.

Results: A total of 5,970 annual entries were evaluated (T1, N=3033; T2, N=2937). FF were detected in 25.3% and 27.1% of cases in T1 and T2, respectively (p=ns). *Aspergillus spp.* was the most common species isolated in both periods (93.8% in T1, 80.4% in T2). Adoption of EC did not affect Aspergillus prevalence (23.7% in T1 *vs* 21.9% in T2; p=ns). In contrast, prevalence of NAFF significantly increased over T2 up to 2.7 times compared to T1 (from 2.8% to 7.6%; p<0.001). Most frequently isolated NAFF in both T1 and T2 was Scedosporium (2.2% and 3.7%, respectively); however, the highest relative change in prevalence was recorded for Rasamsonia (17.5 times, from 0.04% to 0.7%) and Exophiala (8.3 times, from 0.3% to 2.5%). Prescription of azole therapy increased significantly from 22.7% in T1 to 29.2% in T2 (p=0.009), with rapid emergence of azole resistance (21.4%). Patients colonised by FF were characterised by significantly worse nutritional status (p<0.001), accelerated lung function decline rate (p=0.024) and higher pulmonary exacerbation rate (p<0.001).

Discussion: Introduction of EC significantly increased detection rate for NAFF, but not for *Aspergillus spp*. Adoption of EC was associated with increased use of azoles and subsequent development of azole resistance. Airways colonisation from FF was associated with significantly worse clinical outcomes.

FROM LAW TO MEDICAL PRACTICE: APPLICATION OF LAW 219/2017 IN REAL LIFE

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Background: On 22 December 2017, law 219/2017 called also "Provisions for informed consent and advance directives" was approved in Italy. This law for the first time governed the legal institution of informed consent or refused medical treatment. Also, introduce two important innovations in the medical context such as shared planning of care and advance treatment directives. Like all innovations also this new law has needed time so that it can be metabolized by physicians who every day are faced with problems regarding the consent or dissent to medical treatment.

Methods: This work is based on a personal case study relating to requests for consultancy received in the current year from the forensic medicine unit of the University Hospital of Modena, which includes two main hospitals: Policlinico of Modena and Civil Hospital of Baggiovara. Globally can count on about 1,108 beds and about 46,430 admissions each year and over 100,000 Emergency room admission. The purpose of the work is to provide an overview of the real-life application of the new law on informed consent, underlining the main critical issues concerning the acquisition of consent that emerged in the period examined.

Results: Based on the first preliminary data, it emerges that more than 2/3 of the consultations requested by clinicians to legal medicine section are related to issues concerning consent or refusal to treatment, problems relating to the natural or acquired inability to provide valid consent, and more rarely problems related to advance directives and/or shared care planning

Discussion: Although the law on informed consent has been in force for several years, clinicians are still far from metabolizing the issue of informed consent. in the current precarious context of the Italian health system, which the COVID-19 pandemics has further exacerbated, the analysis of the advice required of legal medicine on the subject of informed consent still shows a picture that is far from perfect. The analysis of the consultations requested by clinicians can therefore represent a valid tool for identifying any critical issues on which to intervene by adopting training sessions to pursue a continuous improvement of care and the full protection of the patient's right to self-determination.

THE EFFECT OF PHYSICAL ACTIVITY ON MENTAL HEALTH IN PATIENTS WITH ALZHEIMER'S DISEASE

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Background: Alzheimer Disease (AD) is the main cause of dementia. Dementia has been described as the greatest global health challenge in the 21st Century on account of longevity gains increasing its incidence, escalating health and social care pressures. The prevalence of cognitive impairment and dementia is expected to increase dramatically as the population ages, creating burdens on families and health care systems. Several meta-analyses of observational studies suggested a protective effect of physical activity for cognitive decline and risk of dementia and AD. The aim of this study is determine the effect of physical activity on mental health of patients with Alzheimer.

Methods: This protocol describes the methods for a cross-sectional study that will be conducted in Iran, Italy, and Colombia in 2021. For each population information on gender, age, physical activity, lifestyle, life expectancy, quality of life will be gathered through self-administered paper and pencil as well as online questionnaires. IBM SPSS statistics 24 will be used to store, re-code, and analyze all data. Descriptive and inferential statistical methods will be applied. For each group, age (mean) and gender distribution will be reported. Chi-square test and Mann-Whitney U test (continuous variables) will be used to describe the sample and compare characteristics between Alzheimer s patients of each country. Kolmogorov-Smirnov, Spearman correlation coefficient, Kruskal-Wallis, one-way analysis of variance, multiple regression equation with Tukey post hoc tests will be performed to analyze the finding ($P \leq 0.05$).

Expected results: At the end of this study, it is expected that there will be an improving association between Physical Activity, Health-related quality of life (HRQOL), Lifestyle behaviors, Life expectancy in AD patients. Also, we will compare the data of Iran and Italy, and Colombia together and will evaluate the quality of life in patients with Alzheimer's in three different continents with different situations.

Discussion: The aim of this project to identify patients in a pre-symptomatic stage for early treatment to delay progressive cognitive decline and disease onset and to development of new diagnostic markers of Alzheimer's disease. The study might be limited due to bias in self-reporting concerning the quality of life, lifestyle habits, physical activity, and life expectancy. Also, the results may not be generalizable to all patients with AD. patients with more impairment in AD, less physically fit patients, or patients with more comorbidities 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.

USE OF HYDROGEN AS A CARRIER GAS AND CHEMICAL IONIZER FOR THE DETERMINATION OF PCBS AND PAHS IN GC/NICI-MS

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Background: Polychlorinated Biphenyls and Polycyclic Aromatic Hydrocarbons are classes of organic compounds that include hundreds of chemical species. Among these, only a few isomers are involved in environmental and food analytical studies, given their classification as proven, probable or possible human carcinogens by the IARC. These compounds are classified according to the Toxic Equivalent Factor (TEF) which refers to 2,3,7,8-TetraCloro-p-Dibenzo Dioxin for PCBs and Benzo (a) pyrene for PAHs. Generally, planar compounds or ones having “bay regions” show a higher TEFs. According to literature there is a correlation between the carcinogenicity of compounds and their electrophilic character. In fact, electrophilicity favors the formation of adducts with DNA.

Objectives: The aim of this research is to develop a simplified, rapid and selective analytical GC/NICI-MS technique using H2 both as carrier and reagent gas to discriminate carcinogenic compounds from non-carcinogens based on their electrophilicity. Currently the only existing technique to separate the two groups is through the clean-up phases depending on chemical characteristics (mainly planarity). Alternatively, slow chromatographic runs can be used to separate each individual isomer, but lengthening the analysis time.

Results: Using hydrogen as a reactant in negative chemical ionization, surprising results have been achieved. This chemical ionizer has been shown to be able to enhance the electrophilic potential of the analytes, as demonstrated in the application on the classes of PCBs and PAHs. A selective GC/NICI-MS response was observed for planar PCBs (non-ortho or monoorto) and for PAHs with a "bay region". This specific carcinogenic selectivity has the advantage of reducing clean-up operations during the laboratory processing of the sample and avoiding possible overestimations due to the coelution of non-toxic isomers. The most important result is the surprising proportionality between the TEFs of the individual substances and the GC/NICI-MS response factors obtained with hydrogen as a reagent gas. Furthermore, the halving of analysis times and consequently of costs by using hydrogen as carrier gas instead of helium should not be underestimated.

Future perspectives: The main goal of this research is the possibility of having an analytical system of early warning to identify possible carcinogenic substances. Furthermore, this technique allows to deepen the knowledge on the mechanisms that regulate carcinogenic processes. Future studies foresee the fundamental step of confirming the applicability of the GC/NICI-MS technique on other classes of analytes starting from the POPs indicated by the Stockholm Convention (whose carcinogenicity

is already ascertained). The next step will therefore be to apply this technique to the study of Untargeted compounds (in addition to those targeted) allowing to have a preliminary screening on their carcinogenicity and to identify new classes of emerging contaminants.

MODULATION OF PHENYLALANINE AND TYROSINE METABOLISM IN HIV-1 INFECTED PATIENTS WITH NEUROCOGNITIVE IMPAIRMENT: RESULTS FROM A CLINICAL TRIAL

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Background: HIV population is still facing a high prevalence of non-AIDS defining conditions related to the high levels of immune activation. Growing evidences support the role of gut resident bacteria in the pathogenesis of the persistence of immune activation and in the onset of neurologic disorders like major depression and autism. Phenylalanine and tyrosine represent precursors in the pathway of the synthesis of catecholamines, thus alterations in their metabolism could lead to a reduced cognitive performance. Alterations of phenylalanine/tyrosine ratio have been observed in deferent inflammatory conditions such as sepsis, cancer as well as in HIV infection. With the present study we aimed to evaluate the effect of supplementation with oral probiotics on phe/tyr metabolism as its effect on neurocognitive function of HIV-1 infected individuals.

Methods: To investigate the effects of oral bacteriotherapy on intestinal phenylalanine and tyrosine metabolism, in this longitudinal, double-arm trial, 15 virally suppressed HIV+ individuals with subclinical cognitive alteration underwent blood, Cerebrospinal Fluid (CSF) and fecal sample collection at baseline and after 6 months of oral bacteriotherapy. A baseline fecal sample was collected from 15 healthy individuals and served as control group for the baseline levels of fecal phenylalanine and tyrosine. CD4 and CD8 immune activation (CD38+) was evaluated by flow cytometry. Amino acid evaluation on fecal samples was conducted by Proton Nuclear Magnetic Resonance. Neuroinflammation was evaluated by ELISA assay of CSF neopterin levels. Lastly at baseline and after 6 months of oral bacteriotherapy a trained neuropsychologist carried out several neuropsychological tests to assess neurocognitive performance.

Results: A significand reduction in phenylalanine/tyrosine ratio (Phe/Tyr ratio T0: µmol/g 13,6 *vs* T6: µmol/g 4,23; p=0.002), peripheral CD4+ CD38+ activation (median values: T0: 7.65% *vs* T6: 4.11%; p=0.012) and neuroinflammation (Neopterin concentration mean value: 29.29±13.8 nmol/L; T0 *vs* T6, p=0.002) was observed at the end of oral bacteriotherapy. Moreover, at T6, all participants showed a normal neurocognitive performance with significant improvements observed in several of the performed tests.

Conclusion: Given the strong connection between the CNS function and the intestinal microenvironment, the analysis performed in this study aimed to obtain more insights into the gut–brain axis and to understand if and how probiotics could impact on this complex bidirectional crosstalk.

SUBLETHAL EFFECTS ON ZEBRAFISH EMBRYOS SUPPORTING HUMAN HEALTH PROTECTION

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Background: Toxic substances and anthropogenic contaminants are ubiquitous in the environment. They are often present in low concentrations and in mixture with other substances. The overall effects are often unknown or underestimated, therefore new, more specific methods are needed to fill the knowledge gap with the purpose to protect human health.

Methods: The aim of the study is to evaluate the efficacy and sensitivity of sublethal endpoints than lethality in fish embryos, in order to detect the effects of mixtures of contaminants in environmental samples. For this purpose, some of the most occurrent endpoints have been selected: skeletal deformities, organism length, shape of the eyes, spontaneous coiling activity of tail, and heartbeat. Different environmental samples, mainly from rivers and canals, were tested with the acute Fish Embryo Toxicity (FET) test (OECD 236) and in parallel with the measurement of sublethal endpoints. Through the use of the Danioscope software, it was possible to acquire the data in more detail, minimizing the interpretation error.

Results: The preliminary results showed the presence of sub-lethal effects in samples even without acute toxicity. In particular, malformation and the changing in the burst number of coiling tail movements seem the most relevant effects detected. Furthermore, the increasing of burst numbers after 24 hours was mainly correlated to the environmental samples with major acute toxicity obtained after four days FET test.

Discussion: The use of sublethal tests, such as those used in this study, are very useful in the prevention of human health adverse effects as they have proved to be rapid and sensitive compared to acute tests which often require more exposure time. Furthermore, the detection of sublethal effects can be correlated to the presence of contaminants that show these particular modes of action (e.g., embryotoxicity, neurotoxicity) that are relevant also for human health. These tests could represent a valuable contribution to identify risks of emerging contaminants and mixtures in the ecosystem potentially harmful to human health.

ANABOLIC ANDROGENIC STEROIDS (AAS) AND ORGANS DAMAGE: STUDY OF NANDROLONE TOXICITY ON ENCEPHALUS IN AN ANIMAL MODEL

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Background: Anabolic-Androgenic Steroids (AASs) are a large group of molecules including endogenously produced androgens, such as testosterone, as well as synthetically manufactured derivatives. AAS use is widespread due to their ability to improve muscle growth for aesthetic purposes and athletes' performance, minimizing androgenic effects. However, AASs have side effects, involving all organs, tissues and body functions, especially long-term toxicity involving the cardiovascular system and the reproductive system, thereby, their abuse is considered a public health issue.

Objectives: project aim is to clarify the morphological effects of prolonged use of AAS in a mouse animal model, focusing on the apoptotic mechanism and on the brain areas involved in the behavioral effects, memory and emotional aspects.

Expected (or preliminary) results: In this experimental study, male rats were divided into 4 groups of 6 rats. All animal experiments were conducted in accordance with national guidelines and protocols, approved by the Institutional Animal Ethics Committee (IAEC no.03/028/07). 6 mice trained with nandrolone decanoate dose of 1.875 mg/kg; 6 sedentary mice with nandrolone decanoate dose of 1.875 mg/kg; 6 vehicle-treated trained mice; 6 sedentary vehicle-treated mice. After the animals were sacrificed, brain samples were taken from each mouse for histological analysis, focusing attention on the frontal cortex and hippocampus. Staining was carried out with haemetoxylin and eosin and immunoreaction with the caspase 3 antibody. Expression of caspase-3 antibody staining was also recognized as negative or positive. Discoloration defined by immunohistochemistry was distinct as was recognition of the brown chromogen within the cytoplasm and / or nucleus. Apoptosis and oxidative stress are common mechanisms in all organs involved in organ damage mediated by AAS. These mechanisms are also involved in brain damage and neurodegeneration, particularly in the frontal region and hippocampus, therefore, in the long-term sequelae of AAS abuse. Caspase 3, being an executing caspase, is a reliable marker for organ damage and activation of the apoptotic process at the brain level.

Future perspectives: The scientific community should intensify its efforts to clarify the pathophysiology of behavioral disorders and cognitive impairment due to long-term exposure to AAS. Further studies are urgently needed to support the development of a

reliable diagnostic tool to identify early AAS abuse as well as a therapy based on robust scientific evidence. Information and education are fundamental tools for preventing the abuse of AAS.

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

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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, were 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 (2017-2021) 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 sites known for the presence of An. maculipennis s.l. and the host choice assessed by molecular blood meal analysis of engorged mosquitoes collected. Comparative trap performance in collecting Anopheles was also evaluated in two sites.

Results: In total, 79/94 (84.0%) sites monitored for adult mosquitoes were positive for Anopheles species. They were found mainly in rural-suburban sites as animal shelters (82.4%) and warehouses (10.8%). In total, 2,416 adult Anopheles were collected, mostly belonging to An. maculipennis complex (98.8%). The highest density recorded was about 900 specimens/sampling. PCR analysis performed on 1405 An. maculipennis s.l. adults showed the presence of An. messeae/daciae (82.4%), An. maculipennis s.s. (19.9%), and An. atroparvus (0.7%). Anopheles spp. larvae were found in 22/31 sites (71%). Seven An. messeae/daciae were caught in six HLC. Among fed specimens collected (115 An. messeae/daciae and 12 An. maculipennis s.s.), one human blood meal was identified in An. messeae/daciae even if the most chosen host was horse (n=52).

Discussion: Despite the absence of historical main malaria vector in this area (An. sacharovi), our findings show that secondary malaria vectors are still present in northeastern Italy, locally abundant with higher density during the late summer. An. messeae/daciae is the most common species, occurring mainly around Venice lagoon and Po River. Even though generally zoophilic, this mosquito bite also humans; therefore, the potential risk of malaria autochthonous cases/outbreak sustained by this species is very low but not impossible.

DETERMINING THE ROLE OF BLOOD BIOMARKERS, IMMUNE CELLS AND TOCILIZUMAB AS AN EFFECTIVE IMMUNO-MODULATOR DURING THE COURSE OF COVID-19 PNEUMONIA

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Background: Emerging evidence argue that cytokine storm, monocytes, circulating innate immune cells, are principal players in COVID-19 pneumonia. The study aimed to investigate the role of soluble sCD163 and sCD14 plasmatic levels in predicting disease severity, characterize peripheral blood monocytes and Dendritic Cells (DCs), study tocilizumab as a potential immunomodulator in patients with COVID-19 pneumonia (COVID-19 subjects).

Methods: 219 subjects (172 COVID-19 positive (ARDS and non-ARDS) and 47 Healthy Donors (HDs) were enrolled in the study. COVID-19 was confirmed by RT-PCR. Clinical parameters included age, sex, comorbidities such as hypertension, neoplasia, cardio vascular diseases, Ventilation etc. Plasmatic levels of sCD163 and sCD14 were evaluated using kit ELISA (R&D systems). Multiparametric flowcytometric methods were used for characterization of peripheral blood monocytes and Dendritic cells. Longitudinal effects of Tocilizumab on Plasmatic sCD163 were analysed at Baseline(T0), 7 days Post therapy (T7) and further at follow-up (T45) in a subgroup of 45 ARDS patients treated with tocilizumab (Responders and Non-Responders) and 25 Controls (non-tocilizumab treated). Ferritin, D-Dimer, LDH, P/F and CRP were administered immediately after admission.

Results: Compared to HDs, COVID-19 subjects showed higher sCD163 ($p<0.0001$) and sCD14 ($p<0.0001$) plasmatic levels. ARDS group showed higher sCD163 plasmatic levels compared to the non-ARDS ($p=0.002$). Baseline sCD163 values were also significant in tocilizumab treated patients compared to the control group ($p=0.02$). sCD163 decreased longitudinally in both tocilizumab responders and non-responders ($p=0.02$) while no differences were observed in the control group. Compared to HDs, COVID-19 subjects showed lower percentages of non-classical ($p=0.0012$) and intermediate monocytes ($p=0.0447$), slanDCs ($p<0.0001$), myeloid DCs (mDCs, $p<0.0001$), and plasmacytoid DCs (pDCs, $p=0.0014$). The non-ARDS group showed lower percentages of non-classical monocytes ($p=0.0006$), mDCs ($p=0.0346$), and pDCs ($p=0.0492$) compared to the ARDS group. P/F at baseline and P/F nadir were significant in all COVID-19 Patients ($p<0.0001$). Ferritin, D-Dimer, LDH and CRP were elevated at baseline in all the COVID-19 subjects.

Conclusions: The increase in sCD163 and sCD14 plasmatic levels, observed on hospital admission in COVID-19 subjects, especially in those who developed ARDS, and the correlations of these monocyte/macrophage activation markers with typical inflammatory markers of COVID-19 pneumonia, underline their potential use to assess the risk of progression of the disease. Biomarkers such as Ferritin, D-dimer, LDH and CRP are evident in determining the extent of infection in deciding the line of treatment. Moreover, tocilizumab therapy can be effective in down regulating the concentration of sCD163.

EFFECT AND MODULATION OF *ASPERGILLUS FUMIGATUS* EXTRACELLULAR PROTEINS

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Background: *Aspergillus fumigatus* is the most important airborne mold pathogen and allergen worldwide that causes invasive, chronic, allergic infection and it rarely invades the central nervous system. The mortality rate for the invasive disease is ~50%. *A. fumigatus* secretes numerous proteins and metabolites that help the fungal growth, alter host-signaling processes in human cells and play a critical role in fungal-host interactions and pathogenesis. An extracellular metabolite such as gliotoxin induces toxic effects on different brain cell types. To date, there are no studies on the effect of *A. fumigatus* extracellular proteins on brain cells. For *A. fumigatus*, only a limited number of established targets and corresponding drugs are available. The extracellular proteins involved in virulence could be a target. Protein expression is controlled through epigenetic regulation. In fungi, BET family proteins regulate the transcription of >500 genes.

Objectives: Study the *A. fumigatus* extracellular proteins and their activity on astrocytes and neurons. Study the modulation of extracellular proteins effect using JQ1 a BET family inhibitor and their activity on *Galleria mellonella* larvae, an alternative *in vivo* model to study fungal virulence and pathogenicity.

Results: The results obtained from the study of the activity of *A. fumigatus* extracellular proteins on primary culture astrocytes and neurons showed a dose-dependent activity of *A. fumigatus* extracellular proteases on astrocytes and neurons. The astrocyte's exposure to 35 kDa *A. fumigatus* extracellular protein significantly increased the level of IκB kinase phosphorylation. Moreover, the results demonstrated, with immunocytochemistry analysis, the migration of NF-κB 65 and NF-κB 100 in the nucleus of the cells. Among the modulation of extracellular proteins, different epigenetic modulators are used. The best results are obtained with JQ1. JQ1 showed MIC50 values >100 μM. JQ1 significantly reduced the concentration of extracellular proteins at a concentration of 100 μM. Preliminary results obtained with LC-MS/MS assay, have shown the reduction of some virulence proteins such as allergen Asp f 15, neutral protease, peptide hydrolase, glucan endo-1,3-beta-glucosidase. Studies *in vivo* with larvae of *G. mellonella* has demonstrated that the protein obtained after treatment of *A. fumigatus* with JQ1 decreased the mortality by 50% and decreased the melanization of larvae haemolymph.

Future perspectives: It will be studied the activity of JQ1 and other inhibitors on Bdf1 *A. fumigatus* BET proteins as a new target for Aspergill.

THE IMPACT OF CYTOMEGALOVIRUS IN MULTIPLE SCLEROSIS: IMPLICATIONS FOR NATURAL KILLER CELL REPERTOIRE

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Background: Cytomegalovirus (CMV) has been associated with a lower Multiple Sclerosis (MS) susceptibility based on seroepidemiological studies. In MS patients treated with Disease-Modifying Therapies (DMT), CMV can be related to several complications. CMV chronic infection leads to marked changes in the immune system of the host, including an adaptive differentiation and persistent expansion of an NKG2C+ Natural Killer (NK)-cell subset with high cytotoxic activity and increased immunoregolatory function. Aim of the study was to assess the presence of CMV in MS patients and investigate whether the CMV-induced changes on NK subset can influence the clinical course of MS.

Methods: At the Neuroinfectious Unit of Policlinic Umberto I, Sapienza University of Rome, MS patients were enrolled. Before starting or switching to DMT, for each patient serological and molecular CMV evaluation was performed. By flow cytometry, NK cells were characterized as followed: NK CD56bright, NK CD56dim, NK CD57+, NK CD56dim CD57+, NKG2C Mean Fluorescence Intensity (MFI) on total NK and on NK CD57+. Correlations between NK subsets and clinical parameters were investigated.

Results: 174 MS patients (101 females/73 males) with a median age (IQR) of 49 (40-57), median years of disease of 10 (4-19) and median Expanded Disability Status Scale (EDSS) of 3.3 (1.5-6.0), were enrolled. The 37.9% (66/174) of patients were treatment-naïve while 62.1% (108/174) non-naïve. Among them, 67% (87/129) were CMV seropositive (IgG+/IgM-). No evidence of recent CMV infection were identified. For a subgroup of patients, immunophenotyping of NK was performed. Stratifying this subgroup according to CMV DNA detection (5 CMV DNA+, 6 CMV DNA-), no significant differences were observed in median value [IQR] of cells percentages. For total NK, 9% [1.2-11.3] *vs* 5% [1.2-10.8]; CD56bright, 10.2% [6.6-18.6] *vs* 12% [5.3-20.4]; CD56dim, 87.5% [81-93] *vs* 86.4% [79-93.6]; NK CD57+, 21% [16.2-30.7] *vs* 16.5% [15.2-19.1]; CD56dim CD57+, 22.4 [16.8-39.9] *vs* 17.1 [16.6-20.7]; NKG2C MFI on total NK, 1097 [317-1837] *vs* 1050 [317-1720]; NKG2C MFI on NK CD57+ cells, 1435 [557-2174] *vs* 1206 [634-2352]; respectively in CMV DNA+ *vs* CMV DNA-. Moreover, EDSS was significantly positive correlated both NKG2C MFI on total NK (ρ=0.706, p=0.033) and NKG2C MFI on NK CD57+ (ρ=0.750, p=0.020).

Discussion: In line with other authors, we found that CMV seroprevalence was lower in people with MS. Our results showed that the increase of NKG2C expression on NK cells appeared to be related to disability progression, suggesting a detrimental influence of this subset on MS. However, we did not observe significant differences in NKG2C+ MFI expression, stratifying the patients according with CMV detection.

ENTOMOLOGICAL FACTORS UNDERMINING THE EFFICACY OF INSECTICIDE TREATED BED NETS IN PREVENTING MALARIA TRANSMISSION: EVIDENCES FROM A LONGITUDINAL SURVEY IN A RURAL VILLAGE OF BURKINA FASO

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Background: Long Lasting Insecticide treated bednets (LLINs) are considered by WHO as the main malaria vector control strategy, combining individual physical defense with the collective protection provided by the pyrethroids restrained in net fibers. Despite the success obtained in malaria prevention in the first 15 years from LLINs mass distribution, to date, a stalling of progress in the fight against malaria has been registered in 10 sub-Saharan countries (accounting for approximately 70% of the world malaria burden), where the malaria incidence remains still very high despite the large bednet coverage. Among many causal factors affecting this scenario, mosquito physiological resistance to insecticide is crucial but a non-negligible role is also played by behavioural strategies adopted by vectors to elude the insecticidal effect of the net. Burkina Faso, where LLINs were introduced in 2010, is paradigmatic for the dramatic epidemiological situation and vector insecticide resistance status of West Africa. Here it is presented a longitudinal study conducted in a village of Burkina Faso, aimed to investigate the entomological factors contributing to explain the high malaria burden in a LLIN-covered area.

Methods: Entomological collections have been carried out in Goden village in 2011, 2012, 2015 and 2019, i.e. at the turn of four bednet distribution campaigns. Resting and host seeking Anopheles gambiae s.l. were collected with different sampling methods, thus allowing to record several entomological parameters associated to malaria transmission: Sporozoite Rate (SR); Entomological Inoculation Rate (EIR); Human Blood Index (HBI), rhythms of biting activity, allelic frequency of insecticide resistance (KDR allele) and frequency of 5 SNPs possibly associated to a novel resistance mechanism imputable to a sensory appendage protein (Sap2).

Results and conclusions: The consistently high SR of 5.5-7.1% detected in the local malaria vectors through the years and the EIR of 10 infective bites/person/night assessed in 2015, confirm the high malaria transmission risk in the village. Vectors are also characterized by: i) stable allelic KDR frequencies, ranging from 54 to 58%; ii) heterogeneous increased frequency of SAP2 SNPs over the study period, with a higher fold-change for 2 of them (1.4 and 3.0); iii) altered biting rhythms diverted from the typical peak in middle of the night; iv) opportunistic host choice, as revealed by the HBI observed

in 2011 and 2019 (15.8% and 36.5%). Therefore, in a typical rural village of Burkina Faso a complex concurrence of entomological factors is undermining LLINs collective protection despite 10 years of net usage.

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

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Background: The 2019 WHO document "Promoting the health of refugees and migrants, Draft global action plan, 2019-2023" aims to improve global health by addressing the health of refugees and migrants in an inclusive manner, in any given setting, also strengthening health monitoring and health information systems. The project aims to design and to experience a set 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, and subsequent inclusions and modifications).

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 made different proposals for the gradation of the indicators. A value, from 0 to 3, can be assigned to each indicator on the basis of what is envisaged and implemented at local level for the topic considered. A grid was created and submitted again to the panel of experts from Italian Regions. 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: 12 main topics were identified to be considered for monitoring, corresponding to 12 summarizing indicators. Monitoring has been currently carried out in 12 Italian Regions 6 out of 12 regions fed the entire grid of indicators. For example, indicator 1 (Enrollment to National Health of foreign irregular minors) and indicator 3 (Availability of socio-linguistic cultural mediator in health services) the average of value is 1.7; for indicator 9 (Accessibility of regional cancer screening programs for irregular migrants), average is 0.2.

Discussion: The monitoring activity was obviously affected by the emergency due to the COVID pandemic. It is hoped that the resumption of health activities will allow missing Regions to send the requested data, in order to increase the representativeness of the monitoring. The analysis of the results obtained so far has begun.

ITALY'S PREPAREDNESS FOR THE HEALTH TECHNOLOGY ASSESSMENT OF GENOMIC TECHNOLOGIES

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Background: Following the discoveries of the Human Genome Project, many genomic technologies are becoming available for clinical practice. In Italy, the inclusion of such technologies into the Essential Levels of Care is largely unregulated. In order to identify valuable genomic applications to guarantee as citizens' rights, a standardized and specific Health Technology Assessment (HTA) process is needed. Thus, we aimed to explore Italy's preparedness to use HTA for the regulation of genomic applications.

Methods: We explored the state of HTA in Italy, in general and for genomic technologies, both at a national and regional level. For the national level, we performed a narrative review of the existing policy documents regulating the HTA process and the implementation of genomic technologies, in order to identify the main actors and their roles. For the regional level, we updated a previous survey describing the implementation of HTA across the Italian Regions trough a literature search and a search of institutional websites.

Results: At a national level, five documents regulating the HTA process, both in general and for genomic technologies, were retrieved. The three key national players involved in the governance of the HTA process for genomic technologies are the Ministry of Health, the Italian Institute of Health, and the National Agency for Regional Healthcare Services. Nevertheless, their role and responsibilities are not clearly defined. At a regional level, it emerged that 76% of the Regions has specific regulations for the HTA process, although many differences exist in terms of type of technologies evaluated, methodology used, and type of reports produced. Moreover, we found that no specific strategies for the assessment of genomic technologies are in place at a regional level.

Discussion: At a national level, Italy has a good organizational and methodological basis for HTA. In the last years, an attempt has been made to specifically address the HTA of genomic applications, but is it affected by a lack of clarity regarding intuitional roles and responsibilities. At a regional level, the HTA of genomic applications is not specifically addressed while the HTA of health technologies in general is affected by heterogeneity among Regions.

INALATION RISK ASSESSMENT TO PM COMPONENTS OF THE SOURCES CONTRIBUTIONS IN POLLUTED AREAS BY HIGHT SPATIAL RESOLUTION MAPPING

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Background: PM exposure causes various health problems including premature death in people with heart or lung disease, no fatal heart attack, irregular heartbeat, aggravated asthma, decreased lung function, increased respiratory symptoms such as irritation of airways, coughing, or difficulty in breathing. Terni is one of the most polluted urban and industrial areas in Central Italy. Terni is situated in an intramountain depression and is characterized by the presence of urban and industrial PM emission sources such as vehicular traffic, domestic heating, a power plant for waste treatment and a steel plant. The geomorphological and meteorological conditions limit the dispersion and enhance the accumulation of the atmospheric pollutants. Population is exposed for long period to PM and its components, mainly metals Cd, Cr, Cu, Fe, Mn, Ni, Pb, and Zn. Terni is an ideal area to study inhalation risk assessment by PM e its components correlated to sources contribution by the spatial variability.

Methods: PM concentration and its elemental composition (soluble and insoluble fraction) were measured for the entire year through the acquisition of high spatially resolved data (23 sampling stations in Terni area). Data were elaborated to calculate inhalation risk assessment through accredited algorithms of EPA methodologies for carcinogenic and no carcinogenic metals and for their correlation between different sources and population risks. Risk maps related to the whole urban and industrial area were obtained for children and adult population.

Results: Data show risks for the resident population of adults and children exposed for long period to carcinogenic and no carcinogenic metals (Cd, Cr, Cu, Fe, Mn, Ni, Pb, and Zn) contained in particulate matter and a correlation with main emissive sources (vehicular traffic, domestic heating and industrial emission sources).

Discussion: The results permitted to correlate the concentrations measured with exposure risk (adults and children) to atmospheric pollution in Terni area. They proved the efficiency of the new experimental procedure elaborated for inhalation risk assessment of the spatial variability of PM10 components (carcinogenic and no carcinogenic metals) through the acquisition of spatially resolved annual data and the correlation between main emission sources.

SMALL-RNA ANALYSIS FROM THIRD-STAGE LARVAE AND EXOSOMES PROVIDES THE FIRST MIRNAS CATALOGUE FROM ANISAKID NEMATODES

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Background: Anisakiasis is an emerging fish-borne zoonotic disease caused by third-stage (L3) larval nematodes of the genus Anisakis. Despite its public health relevance, mechanisms of infections are still unknown. Secreted parasitic factors 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: Small-RNA fractions were isolated from three biological samples of L3 and EX of A. pegreffii from Merluccius merluccius (FAO37) and sequenced on an Illumina platform (single-end, 50bp). After trimming and filtering, raw reads were mapped to the Anisakis simplex genome (As14, Wormbase) and then to a collection of hairpins and mature A. pegreffii miRNAs predicted by a double approach: i) in-silico, using hairpins and mature miRNAs from Ascaris suum and ii) miRDeep* software. Mapping reads were used for assembling a catalogue of A. pegreffii miRNAs and for the differential expression analysis by EdgeR. The expression profile of selected miRNAs was validated by Stem&Loop PCR.

Results: A mean of 33 million and 24 million raw reads were obtained for L3 and EX, respectively. After merging miRDeep* and in-silico predictions, we obtained 206 miRNAs, 156 of which showed a match in the samples (76%). So far, most of Stem&Loop RT-PCR confirmed results from sequencing. Forty miRNAs (25.6%) were found significantly differentially expressed (FC>2.0, FDR<0.05) in the pairwise comparison between L3 and EX. Among 13 miRNAs enriched in EX, some showed targets related to immunity and inflammation. The top20 most abundant miRNAs showed seed homologies with other helminths and humans.

Discussion: These results provide the first Anisakis miRNA catalogue, allowing comparative analyses with other parasitic nematodes. Moreover, identification of gene targets in human accidental host may shed some light on mechanisms of host manipulation.

MICROCYSTINS: INTESTINAL ABSORPTION AND BIOTRASFORMATION STUDY BY RECONSTITUTED HUMAN TISSUES

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Background: Microcistyns (MCs) are natural toxins produced by cyanobacteria and they can be found as residues in food and water. The role of transporters in the gastro-intestinal absorption and the toxicokinetic seems to have a crucial role in the toxicity of these compounds. In this study we investigated the transport of four MCs (MC-LR, RR, LW and LF), characterized by different hydrophilicity, using the EpiIntestinal model, an *in vitro* 3D system, reconstituted from human intestinal cells. This system reflects both *in vivo* intestinal barrier anatomy and functionalities including active transport mechanisms. The MCs intestinal absorption was studied by measuring their capability to pass through the epithelium highlighting the mechanism and the specific (absorptive and/or secretory) transporter involved.

Methods: MCs congeners LR, RR, LF and LW were tested at 40 μM. Reference substrates and inhibitors of specific intestinal transport proteins (Pgp, MRP2 and BCRP, as efflux proteins, and OATP 1A2 and 2B1, as absorptive proteins) were used to verify their presence/activity in EpiIntestinal tissues. The rate by which MCs pass through the epithelium and the spontaneous or enzymatic formation of their conjugates with glutathione, the known detoxification pathway, were evaluated with an ad hoc HPLC method.

Results: EpiIntestinal expresses active forms of all the considered transporters. MCs seem to be substrates of both absorptive and secretory transporters. LW is the only variant for which the transport is clearly attributable to OATP 2B1, but not 1A2, the OATPs mainly present in the intestine. For the other congeners results showed that efflux and absorption transports are involved at the same time. Furthermore, no glutathione conjugates were detectable neither into the cells nor in the medium.

Discussion: MC congeners are absorbed by intestinal epithelium with different rate. LW is transported by OATP 2B1 and not by 1A2, while the other congeners seem to be substrates of transporters, both secretory and absorptive, involved at the same time. These opposite and contemporary fluxes and the overlapping in specificity of action of most of the available known inhibitors, make results not able to identify each specific transporter involved. Western blot analysis, to verify the expression of transporters in the EpiIntestinal model, have been planned and will help in the unambiguous knowledge of all the involved mechanisms of transport. The lack of MC-glutathione conjugates detection seems to indicate a low metabolic capability of the system.

CYTOKINE STORM IN COVID-19-RELATED DEATHS: FROM SARS-COV-2 RNA DETECTION TO IMMUNOHISTOCHEMICAL QUANTIFICATION OF PROINFLAMMATORY CYTOKINES IL-1B, IL-6, IL-15 AND TNF-A

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Background: Current evidence suggests that a cytokine storm is the major cause of ARDS and multiple organ failure, and is consistently linked with fatal outcomes. Also SARS-CoV-2 infection is characterized, in the early stages, by initial local inflammatory response to the virus infiltrates and progressive parenchymal lung damage, while a systemic inflammation damage can occur when the host inflammatory response continues to amplify.

Aims: The aim of this study is to clarify the correlation between SARS-CoV-2 infection and the inflammatory response, to evaluate the tissue localization of the virus in various organs and to investigate the expression of cytokines/chemokines (IL-1β, IL-6, IL-10, IL-15, TNF-α, MCP-1), leukocyte markers (CD4, CD8, CD20, CD45) and fibrinogen, in an attempt to verify and define the role of cytokines in COVID-19-related deaths.

Methods: In all the selected cases SARS-CoV-2 RT-PCR was performed on swabs collected from the upper (naso-oropharynx) and/or the lower respiratory (trachea and primary bronchi). A total of 60 SARS-CoV-2 positive subjects and 20 controls were included. Histological (hematoxylin–eosin staining) and immunohistochemical semi-quantitative analysis were performed on the multiorgan samples taken during autopsy. Tissue localization of SARS-CoV-2 was detected using antibodies against the nucleoprotein and the spike protein. The presence of viral particles was assessed using electron microscopy.

Results: Immunohistochemical staining showed that endothelial cells expressed IL-1β in lung samples obtained from COVID-19 group ($p<0.001$). Similarly, alveolar capillary endothelial cells showed strong and diffuse immunoreactivity for IL-6 and IL-15 in the COVID-19 group ($p<0.001$). TNF-α showed a higher immunoreactivity and CD8+ T cells where more numerous in the lung samples obtained from COVID-19 group ($p<0.01$). Electron microscopy revealed viral particles within the cells of the lungs, trachea, kidney, and large intestine.

Discussion: Our study highlighted the morphological impact of the cytokine storm triggered by SARS-CoV-2 infection and the potent inflammatory response involved in the pathogenesis of COVID-19. We have experimentally confirmed that proinflammatory cytokines, such as IL-1β, IL-6, IL-15, and TNF-α, are produced at sites of tissue inflammation, determining a specific immune response. However, further autopsy studies are needed to expand this evidence and highlight the pathophysiology of SARS-CoV-2 infection.

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

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Background: In recent years, the synthesis and introduction into the illicit market of New Psychoactive Substances (NPS) has reached alarming levels. More than 790 compounds have been identified by the European Monitoring Center for Drugs and Drug Addiction. In this context it is essential to have the right tools to identify these recent NPS and verify their consumption. Among the newest NPS, synthetic opioids deserve special attention, in particular fentanyls, which covered more than 70% of the opioid's world demand.

Methods: The aim of the project involves the characterization of new fentanyls, the identification of their main metabolites and the development of innovative, fast and simple analytical methods, for the determination of these compounds in different biological matrices. Thanks to its high versatility and performances, UHPLC-HRMS/MS was used to characterize, identify and quantify the target analytes.

Results: Thanks to the collaboration with National Police Forces, two new fentanyls, found in seizures, were characterized, by means of the application of different analytical techniques. Furthermore, metabolic pathway of these new opioids was ascertained by means of *in silico, in vitro*, *in vivo* and *ex vivo* studies. Analytical methods for the identification of these analytes in different biological matrices were also developed and validated. Miniaturized preparation technique, such as Micro Extraction by Packed Sorbent (MEPS), Parallel Artificial Liquid Membrane Extraction (PALME), Dispersive Liquid-Liquid Micro-Extraction (dLLME) were optimized for the analyses of tissues, whole blood, plasma, oral fluid and urine. All methods involve the use of a small amount of biological sample (100 µL of biological fluids or 1 mg of tissues).

Discussion: Thanks to the application of different analytical techniques, and to the development of new analytical methods, we have broadened the knowledge about this class of NPS, enabling the identification of fentanyls consumption and providing an effective contribution to the estimation of their real propagation in Italy.

BAYESIAN STATISTICAL MODELS TO EVALUATE THE EFFICACY OF TRADITIONAL AND INNOVATIVE MOSQUITO CONTROL INTERVENTIONS

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Background: During the last year of PhD project, we worked on the application of Bayesian regression approaches to assess the efficacy of conventional and innovative mosquito control interventions, with the aim to optimize mosquito control management. In particular, we exploited the flexibility of the Bayesian approaches to analyze results of two field experiments conducted in Italy: Exp1) a conventional larval control intervention by a novel combination of *Bacillus thuringiensis* subsp. israelensis and *Bacillus sphaericus* (Bti+Bs) in ditches representing the main larval habitat of *Culex pipiens*, the main West Nile virus vector in rural areas; Exp2) an innovative approach to reduce abundance of adult *Aedes albopictus* based on the release of incompatible males transinfected with a foreign Wolbachia (ARwP) endosymbiont.

Methods: In Exp1, we assessed larval abundance in 5 Bti+Bs-treated *vs* 7 untreated diches in Padova Province. In Exp2 we assessed fertility of eggs before, during and after release of ARwP males in a treated green area and in an untreated ecologically similar area in Rome. Generalized Additive Mixed Models (GAMM) were developed to model the observed either larvae/pupae (Exp1) or viable egg (Exp2) abundance overtime, accounting for multiple locations and repeated samplings. A two-stage Generalized Linear Model (GLM) was developed for Exp2 to infer the exposure of field-collected females to mating with released ARwP-males.

Results: GAMM results showed: in Exp1, a dramatic reduction in larval abundance already 24h post-treatments (93%) with lack of living larvae up to 22 days and high residual effect in pupae density up to 39 days (84% after 39 days); in Exp2, a lower percentage (up to 35%) of viable eggs in treated than in control site, with approximately 22% of females collected near the release spots showing 100% sterility and an overall ARwP/wild-type ratio >1 (1.12:1).

Discussion: Our results show how the application of novel Bayesian regression approaches to the evaluation of mosquito control intervention allows obtaining important quantitative results from field experiments, such as the comparison of the mosquito temporal pattern between treated and control sites and the estimation of the overtime mating exposure of wild females with released ARwP-males. The results support the added value of collaboration between statisticians, entomologists and public health officers in order to better exploit experimental results by advanced statistical tools and provide valuable data for the evaluation and planning of mosquito control.

Virtual Poster Session

FORENSIC APPLICATION OF MONOCLONAL ANTI-HUMAN GLYCOPHORIN A 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.

Methods: On all sample collected during autopsy, 4 μm-thick paraffin-embedded sections were cut and stained with H&E staining following the standard protocol. In addition, anti-human GPA antibody immunohistochemistry investigation was performed using antibodies anti-glycophorin A. Pre-treatment was necessary to facilitate antigen retrieval and to increase membrane permeability to antibodies anti-glycophorin A boiling 0.25 M EDTA buffer, at 20°C.

Results: 10 cases were selected analyzing the documentation of peculiar autopsies performed by the Institute of Legal Medicine of Rome from 2010 to 2020: 5 samples of fractured bones (cranium, vertebra, mandible, and rib) and 5 samples of soft tissues (soft tissue of larynx, skin in the neck region, and retina). 3 cases were enrolled as controls: femoral fracture, neck skin and tracheal soft tissue. Monoclonal antibodies against GPA resulted positive in 8 of the analyzed cases, indicating the presence of RBC and demonstrating the vitality at the moment of the lesion. In 2 cases, anti-human GPA antibody immunohistochemistry investigation was found negative. Equally, the results in the control cases have been negative.

Discussion: The preliminary results suggest that the use GPA immunohistochemical staining should be routinely applied in cases of corpses with advanced putrefaction phenomena, even when the radiological investigation, the macroscopic investigation and the H&E staining are not reliable. Though certainly not conclusive, this experimental application demonstrated that the use of monoclonal antibody anti-human GPA on bone and soft tissues could be important to verify whether the lesion is vital or not. Even though, it is necessary to investigate if this method is applied to the putrefactive neck skin in hanged individual.

INFLAMMATORY MECHANISMS IN CACO-2 CELLS STIMULATED WITH ANISAKIS-DERIVED MESSENGERS OF PATHOGENICITY

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Background: Anisakiasis is a zoonotic disease caused by consumption of raw fish parasitized with Anisakis spp third stage larvae (L3). Larval migration in the gastrointestinal tract, the excreted/secreted products and Extracellular Vesicles (EVs) can progressively determine allergic symptoms, erosive ulcerous lesions and granulomas. Reports of tumors co-occurrence with Anisakis L3 are increasing but pathogenic mechanisms, role of host's immune response and potential implications are still unknown. The aim of this study was to investigate the inflammatory pathway in in-vitro human epithelial colorectal adenocarcinoma cells (Caco-2) exposed to the live L3, the Crude Extract (CE) and the exosomes enriched fraction, as representative of mechanical action of larval motility, whole body of senescent larvae and inflammation silencing, respectively. In particular, the activation of inflammatory response key molecules (ERK1/2, NF-kB), and the amounts of the pro-inflammatory cytokines (IL-6, IL-8) were analyzed.

Methods: L3 collected were used for incubation as live L3, for CE preparation and for EVs isolation. Samples were incubated with Caco-2 cells (6h/24h) at 37°C in the presence of 5% CO2. Cell lysates were used for Western Blot (WB) and supernatants were used for ELISA tests.

Results: Caco-2+L3 showed a progressive decrease of IL-6 ($P<0.01$) and IL-8 if compared to non-treated cells. Differently, in Caco-2+EVs, IL-6 was not detected ($P<0.01$) and IL-8 was strongly downregulated ($P<0.01$). On the contrary, CE induced a strongly increased secretion of IL-6 ($P<0.01$) and a decreasing trend in IL-8. Accordingly, WB analyses showed an increased phosphorylation level of ERK1/2 in Caco-2+CE ($P<0.05$) and in Caco-2+L3, with a slight increased level of activated NF-KB. No differences were observed in the phosphorylation levels of ERK1/2 in cells incubated with EVs compared to the controls.

Discussion: The results obtained showed an intricate host-parasite interplay, characterized by an early phase where active L3 and its released EVs modulate the immune response to find a long-lasting niche, and a later/tardive phase where L3 senescence may lead to the activation of host immune

VIOLENCE AGAINST HEALTH WORKERS: THE IMPACT ON PSYCHOPHYSICAL WELL-BEING AND WORKING ACTIVITY

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Background: The aim of the project is to monitor and analyze the phenomenon of violence against health workers at the Sant'Andrea Hospital in Rome evaluating the impact of the violence on the psychophysical well-being of health workers as well as its impact on their lifestyle and working activity. We will further evaluate to what extent and how these effects may reduce work performance.

Methods: The study must include a research group, a study population, assessment tools to be used, including the Svbpa (Scale of assessment of psychological well-being after the attack). The innovative idea consists in creating a questionnaire, in collaboration with the Psychologist of the Health Department. The health workers will fill in again the questionnaire including information about the change in psychophysical conditions over time and the repercussions on the work activity after a specific time from the event. The results will be analyzed through a statistical processing of the collected data.

Results: The expected results consist primarily of involving as many victims as possible. Secondly, it is proposed to identify what the individual consequences linked to the phenomenon are by separating physical and psychic consequences, as well as its intensity evolution in terms of quantity and quality of time. At least, identify the long-term effects of the event, the type of violence that has the greatest impact on the psychophysical well-being and long-term behavior of the healthcare worker and the reflection of its effects and related consequences in terms of work organization.

Discussion: Increase awareness and knowledge of the phenomenon on the part of health departments by providing interventions on the health worker through training courses on the management of the aggressive user, but also concrete interventions of psychological support even after a long time from the episode, when necessary and when the consequences of the phenomenon are more serious. In addition, in case of new violence events, the statistical data processing program currently in use will be updated and implemented in order to create a usable and accessible tool to evaluate and update the spread of the phenomenon. A further application extension of the project also provides for a mapping of the phenomenon in other hospitals.

VALIDATION OF A NEW MOLECULAR TOOL TO STUDY MALARIA TRANSMISSION THROUGH THE ANALYSIS OF THE ANOPHELES COLUZZII MOSQUITO

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Background: Malaria transmission strictly depends on multiple biological factors related to human host, parasite and mosquito vector. The presence of gametocytes in the peripheral human blood is essential for malaria transmission from human host to the mosquito vector. Human carriers of hemoglobin genetic variants (HbC and HbS) are less susceptible to malaria and simultaneously show an infectious capacity higher than wild type genotypes, contributing to malaria transmission as super-spreaders. Methodological approaches currently employed to study malaria transmission dynamics involve: i) microscopic/ molecular identification of gametocyte stages in the human peripheral blood and ii) identification of parasite's oocysts inside the midgut basal lamina of infected mosquitoes. However, these approaches are constantly hampered by ethical, logistic and practical issues associated to both field and laboratory work.

Methods: This project aims developing a new diagnostic molecular method, based on RTqPCR analysis of single infected An. coluzzii mosquitoes, to investigate malaria transmission mechanisms. Nucleic acids (genomic DNA and total RNA) are extracted from single mosquitoes both to characterize the human genotype and to quantify P. falciparum ookinetes. Using this approach, we aim correlating the load of Plasmodium parasite with the human genetic background. The setting up of this protocol relies on i) the employment of blood fed mosquitoes infected with P. falciparum, collected at different time points spanning the formation and maturation of the ookinete stage inside mosquito midgut and ii) the identification of suitable ookinete-specific markers.

Results: Preliminary data revealed that human genetic polymorphisms are detectable by employing RTqPCR of genomic DNA form single blood fed mosquitoes up to 24 hours post blood-feeding, corresponding to ookinete invasion of midgut basal lamina. Ongoing experiments are focused on the validation of ookinete-specific-markers: stage-specific P. falciparum gene expression profiles were analyzed at 12, 18, 24 and 36 hours post infection, time points corresponding to early, middle, mature and tardive ookinete stage.

Discussion: Malaria transmission is currently studied separately in the human and mosquito host. Here we propose the use of mosquitoes as biological container of the genetic information of all malaria cycle components (human, parasite and mosquito). From previously published transcriptomic data, we have selected 4 microneme associated proteins (CTRP, WARP, SOAP, CHT1) showing ookinete-specific expression profile. We attempt to use these genes as molecular markers for ookinete identification and

quantification inside infected An. coluzzii mosquitoes. This work will provide a novel technical tool to investigate malaria transmission and human host-vector-parasite interplay in future field studies.

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 regarding pediatric patients. 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.

Methods: We performed a retrospective observational study at the Paediatric Intensive Care Unit (PICU) of a large Italian Hospital collecting microbial isolates from 2017 to 2019. We enrolled patients under 18 years of age with an infection due to GN bacteria and a control group of patients without infections. Subsequently, we divided them into groups according to the sensitivity of isolates and we compared them to assess risk factors and outcomes.

Results: We enrolled 68 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 MDR, 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 ≥ 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 ($p=0.010$). We did not observe deaths, but the length of hospitalization was significantly longer in the groups of patients with a GN infection ($p<0.001$) in particular those with CR-GN compared with CS-GN ($p<0.001$)

Discussion: Antimicrobial resistance is an emerging problem even in the pediatric population. Optimization of antibiotics use and improvement in the management of medical devices could be a strategy to try to prevent CR-GN infections in children.

SURVEY ON VACCINE HESITANCY AND HEALTH LITERACY ABOUT VACCINATION AMONG STUDENTS' PARENTS IN A LOCAL HEALTH UNIT OF ROME, ITALY

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Background: Vaccinations represent one of the best tools in Public Health to curb the phenomenon of infectious diseases spread. According to some data from the Eurobarometer report "Europeans attitudes towards vaccination", in Europe, 85% of citizens believe that vaccines are effective in preventing infectious diseases (78% in Italy), and almost half are afraid of severe side effects (48% Europe *vs* 46% in Italy). These beliefs raise what the WHO calls Vaccine Hesitancy, i.e. the delay in accepting or refusing vaccines despite the availability of the vaccination service, a complex phenomenon that needs to be monitored and studied. This study aims to evaluate, through a survey administered to the students' parents of the Local Health Unit (LHU) "Rome 1" (Rome, Italy), the level of health and vaccine literacy and the level of vaccine hesitancy, both parental and about anti-COVID-19 vaccination.

Methods: A cross-sectional study has been prepared on a sample of students' parents of LHU "Rome 1". Approximately 12,600 parents will be recruited for the study in 30 schools randomly sampled, stratified by Health District and weighted on the school's size, to ensure the presence of at least one school of adequate size for each health district of LHU "Rome 1". The data collection will take place through a Google Form to detect the specific data under study according to the Parent Attitudes about Childhood Vaccines Survey (PACV) and the Health Literacy Vaccinal (HLVa) of adults both validated in Italian.

Results: The study will investigate and describe: i) parents' behavior regarding vaccinations of children; ii) the level of health literacy regarding vaccines; iii) the degree of vaccine hesitancy for COVID-19 vaccines. It will also be aimed at identifying predictors of vaccine hesitancy and vaccination health literacy level and measuring their correlation.

Discussion: Considering the impact that vaccination hesitancy could have on maintaining the vaccination coverage thresholds recommended by institutional sources, investigating its determinants on the school parental population assumes a fundamental value for virtuous governance of public health. It is necessary to identify the prevalence of these factors in the population to carry out advocacy functions to support an adequate awareness-raising process towards vaccines importance also throughout the use of ICT.

TELEMEDICINE IN CARDIOVASCULAR AREA AND CHRONIC PATIENT SUPPORT. A NEW PERSONALIZED MEDICINE

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Background: Telemedicine combines medical and informatics techniques that provide care at a distance by eliminating the barriers of time, place and cost related to access to care; it can be used in different contexts and by all health professionals and represents a true diagnostic-therapeutic health service. Telemedicine is particularly useful in two areas: in cardiovascular diseases such as heart attacks, arrhythmias and ischemia that require constant monitoring of certain vital parameters; in patients suffering from other chronic diseases (diabetes, cancer, stroke, dementia) in which the doctor-patient relationship is facilitated and the patient is supported with various tools in the management of their health status. The application takes place on the territory, in hospitals, in specialist clinics and in those of the GP (General Practitioner).

Methods: The evaluation of telemedicine in the two areas under consideration (cardiovascular disease and chronic diseases) was supported by a thorough review of existing literature in which the response of patients treated in both hospital and territorial facilities was analyzed. The analysis also focused on the technologies used for the transmission of texts (medical records, personal data) or images, files, audio and video used to monitor parameters and symptoms (Holter, ECG, saturation, etc.).

Results: With regard to Cardiology, the most important areas of application of Telemedicine are: early diagnosis, remote control of devices (pacemakers, defibrillators) and telemonitoring of patients with heart failure and arrhythmias. In the presence of acute myocardial infarction, the ability to record an ECG in the early prehospital phase has significantly reduced treatment time and mortality. In the management of the patient suffering from chronic disease, telemedicine improves the quality of life of the patient himself and of those who take care of him (caregiver) because it allows to be assisted at home with medical services equal to those provided in hospital. The constant remote monitoring represents a psychological support and allows to avoid the risk of complications, reducing unnecessary movings and hospitalizations.

Discussion: The results obtained show how the innovative mode of medical care implemented with Telemedicine improves and speeds up the taking charge of the patient, both in emergency-urgency and in all health services aimed at the management of the chronically ill, creating new paths of prevention in which the person is at the center of all care mechanisms. The care network is strengthened, patients feel supported, protected and more autonomous in the path of the disease, improving considerably both physically and emotionally.

ENHANCE PRIMARY CARE THROUGH FAMILY AND COMMUNITY HEALTH NURSES. PRELIMINARY RESULTS OF A SYSTEMATIC REVIEW

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Background: The increase in life expectancy, chronic diseases and health needs have shifted the focus from hospital to primary health care, leading to a revolution in the organization of health services. The World Health Organization (WHO) introduced the Family and Community Health Nurse (FCHN) by means of "The Family Health Nurse – Context, conceptual framework and curriculum". The FCHN is a key figure in improving the process of proactive medicine improvement. Due to its recent introduction, it is necessary to identify the results of FCHN practice to enhance their work and assess its effectiveness. The primary outcome of this systematic review was to summarize the evidence regarding the outcomes of FCHN interventions, categorized according to the Nursing Outcome Classification (NOC), to evaluate their effectiveness.

Methods: A systematic review of literature was conducted on databases MEDLINE, CINAHL and Web of Science. We included articles published until March 2020. The review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Results: From 3,492 articles, 98 studies were included. The studies included were mostly RCTs (61 studies) and were conducted in English-speaking countries (40 studies). According to the NOC classification, we systematized outcomes into seven domains: functional health, physiologic health, psychosocial health, health knowledge & behavior, perceived health, family health, community health. The FCHN interventions were effective for the "Functional Health" domain, leading to an increase in Patient-Reported Outcomes (7 studies). For the "Physiological Health" domain, significant increases in Observer-Reported Outcomes were registered (10 studies). The domains on which the FCHN intervention was most effective were "Psychosocial Health" (31 studies) and "Health Knowledge and Behaviors" (35 studies), with an increase in outcomes related to mental health and self-management of health conditions. No statistical significance was found in FCHN interventions for other domains.

Discussion: FCHN interventions are successful in most of the outcomes investigated and they are consistent with the WHO conceptual framework and curriculum. In particular, FCHNs were found to be pivotal in the promotion of family and community well-being, the promotion of health and the management of health conditions. The implementation of FCHN interventions is necessary to enhance community health and the quality of provided care.

COVID-19 HEALTH EMERGENCY AND E-LEARNING: RESULTS FROM THE HEALTH PROFESSIONAL PREPAREDNESS AND RESPONSE COURSE OF ISTITUTO SUPERIORE DI SANITÀ

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Background: Between February 28 and April 28, 2020, the Italian National Institute of Health (Istituto Superiore di Sanità – ISS) launched the first distance course entitled "Health Emergency from the Novel Coronavirus SARS-CoV-2: Preparedness and Response" on the EDUISS platform (https://www.eduiss.it). The course was developed to train Italian healthcare professionals in response to the COVID-19 outbreak. This study presents the first synthetic description and analysis of the training course results.

Materials and Methods: The course included three training units for a total of 16 hours based on the Problem-Based Learning teaching method. E-learning tools were provided by Learning Management System, Totara Learn version 11. Low Interaction, asynchronous mode, and no facilitation were the main technology characteristics. Learning resources including audio-video lectures were developed with the contribution of seventeen experts from various institutions. Each unit included a set of 18 Multiple Choice Questions (MCQs) to self-assess pre- and post-course knowledge improvement. The Continuing Medical Education knowledge final test included 63 MCQs and a satisfaction questionnaire.

Results: A total of 205,830 health professionals enrolled the course and 160,207 participants (74.23%) successfully completed it. Seventy three percentage of participants were enrolled within the first month. The participants who successfully completed the course (completers) belonged to thirty different health professions among which nurses, physicians, physiotherapists, psychologists were the most represented professions. The pre-post data analysis showed that completers significantly improved their knowledge ($t=312.761$, $p=0.00001$) with 94% completers reporting high level of satisfaction on the adopted learning methodology, adequacy of the contents as well as on the e-learning platform functioning.

Discussion and Conclusion: In the first two months of the COVID-19 outbreak, we registered a massive, sudden and simultaneous access of active users on the EDUISS platform. Notably, the total number of participants was more than doubled and significantly exceeded the projected participation rate. Completion rate was also very high especially when compared with the average of the e-learning courses achieved in the previous three years (74% *vs* 66%, respectively). Our results showed that the e-learning course adequately intercepted the training needs of the health care professionals coping with the first stage of health emergency management. Importantly, the course has been internationally recognized and received the prestigious international Totara Award 2020 for "Best Healthcare Project".

THE EXPERIENCE OF THE SARS-COV2 INFECTION IN THE SCHOOLS PLACED IN THE ASL ROMA 3 TERRITORY

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Background: During the first SARS-CoV-2 pandemic phase, the sudden closure of schools has been widely perceived by worldwide people as one of the contributing measures to minimize the spread of the virus. In the second pandemic phase, additional safety procedures have been implemented with the aim of achieving a dual purpose, to guarantee adequate and appropriate educational and social learning to the children, and to ensure continuous prevention and minimization of SARS-CoV-2 transmission in the school setting.

Methods: In the presence of a positive SARS-CoV-2 case, those who have had direct contact with it in the 48 hours preceding the swab or the manifestation of symptoms are quarantined. Information relating to infected cases of SARS-CoV-2 among students and school staff of the ASL Roma 3 territory was collected through an email account dedicated to the management of the COVID-19 emergency within schools and educational services. Data were inserted into a specific database on a daily basis. The data for each case can be divided into three categories: school-related information (name, grade, address and classroom), case-related information (ID, age, type and date of swab, student or school staff), quarantine-related information (start/end date, number of direct contacts placed in quarantine, number of cases that have appeared among the contacts). Only the SARS-CoV-2 cases that led to the quarantine of school contacts were considered. The data collection was performed during the school year 2020-2021 (01 September 2020 - 30 June 2021) and all schools of all levels in the territory of the ASL Roma 3 were considered.

Results: From September 2020 to date, 1550 cases of SARS-CoV-2 have been identified within schools, of which 85% concern students. Cases involving teachers resulted on an average of 32 people being quarantined, compared to 20 people quarantined due to a positive student. The schools most frequently involved with infected cases are lower secondary schools (students 11-13 years). Data collection is still ongoing.

Future perspectives: The data collected will allow to show the distribution of SARS-CoV-2 infection within the schools of the territory considered. Moreover, it will be possible to point out the relationship between the trend of infection in schools and that of the general population in the areas of competence of the ASL Roma3, in relation to the restrictions imposed by the Italian Government.

NEW METHODS FOR MEASLES DIAGNOSIS TO USE IN NATURAL INFECTED AND VACCINATED INDIVIDUALS

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Background: The World Health Organization (WHO) has targeted measles for global eradication through mass immunization. For effective monitoring of eradication targets, high-quality surveillance is needed. The detection of IgM antibodies, specific to the measles virus, with the use of commercial Enzyme-Linked Immunosorbent Assays (ELISA or EIA) is broadly used within the WHO global measles and rubella laboratory network for laboratory confirmation. We will set up an in-house ELISA based on recombinant measles nucleoprotein, which will be used also to develop a medical device by the use of a biosensor capable of detecting in a few seconds the presence in biological liquids of IgM measles antibodies.

Method: The N protein gene will be obtained from purified viral RNA by RT-PCR. In order to run PCR for the viral genome, a set of primers was designed on the nucleoprotein gene using an endemic strain of the measles virus (B3-Dublin). The gene will be cloned in the pGem-T vector and subcloned in the prokaryotic expression vector pQE30 in suitable restriction sites. The protein will have a His-tag at the terminal NH-2 and will be purified by affinity chromatography on NiNTA resin. After suitable production in Escherichia coli e purification, the protein will be adsorbed on electrochemical or fluorescence chips and ELISA Microplates. Measles positive and negative sera from the National Reference Laboratory of Measles and Rubella (NRL) will be used to validate the methods proposed.

Results: A clone of *E. coli* pQE30 was grown overnight in Luria-Bertani broth (LB) agar. pQE30 plasmid was purified using Qiagen miniprep plasmid kit from the bacterial pellet obtained after centrifugation. The purified plasmid was tested on agarose gel electrophoresis in order to verify the presence of plasmid and concentration was determined using a Nanodrop spectrometer.

Discussion: The development of an in-house N-coating ELISA is in line with the current activities of NRL and will allow us to obtain a device with sensitivity and specificity comparable to commercially used kits. Moreover, the development of a device based on biosensors with a conjugate microchip will allow the realization of rapid and economic tests that do not require expensive instruments and specialized personnel, to be used in the “point of care” environment.

ELEVATE TO ALLEVIATE - EVIDENCE BASED NURSING STUDY

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Background: Venous return in the circulatory system of lower limbs results from the interaction of several mechanisms, and reflects the balance between blood inflow and outflow. Blood outflow improves during sleeping because of the lying position especially with leg elevation. In fact, patients with Chronic Venous Disease (CVD) improve leg symptoms in lying position and with leg elevation. The aim of this study is to evaluate the level of comfort of hospital inpatients, without CVD, if they lie with a moderate leg elevation during hospital stay.

Methods: Unselected patients with a hospital stay of at least seven days will be recruited and random assigned to two groups of patients: group A, that will lie in their hospital bed with a moderate leg elevation (between 15 and 30 degrees). Group B, that will lie in their hospital bed without leg elevation. All patients will undergo echo duplex scanning of vascular system of lower limbs to exclude any vascular disease. For every patient complete demographic and comorbidity data will be collected. Every single the day, the following parameters will be retrieved for each patient: ankle and calf diameters, heart rate, blood pressure, breath frequency, body temperature, leg heaviness (rating scale 1-10), perceived leg comfort (rating scale 1-10), hours of night sleep (number).

Results: 20 patients have been enrolled. 10 patients for group A and 10 patients for group B. All parameters were better for group A. Final statistical analysis will be provided the next year at the completion of the study.

Discussion: Our study suggests that if patients during hospital stay lie with a mild/moderate leg elevation they perceive their hospitalization more comfortable.

MONITORING MOSQUITO VECTOR POPULATIONS IN DJIBOUTI CITY: EVALUATION OF A NEW SAMPLING METHOD BASED ON FTA-CARD

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Background: Early detection of pathogens in arthropods is highly important to prevent vector-borne disease outbreaks. However, entomological surveillance methods need constant monitoring, which is expensive in time, cost and labor. In previous years, we modified a BG sentinel trap to keep alive collected mosquitoes through a sugar delivery system. During sugar feeding, potentially infected specimens can release pathogens on a substrate (FTA card) able to preserve nucleic acids for several days in field conditions. This approach simplifies vector surveillance reducing the laboratory procedures for molecular pathogen detection avoiding cool chain.

Methods: In this study the modified BG sentinel trap was tested in 12 sites of Djibouti City (Djibouti). In each site, captures were conducted outdoors for 3-4 days per week from 28th January to 25th February 2020. All collected mosquitoes were morphologically identified and stored, together with FTA cards, in silica gel for subsequent transport to laboratory in Italy. RNA was extracted from FTA cards and currently screened for the presence of Rift Valley Fever Virus (RVFV) by Real Time-PCR.

Results: In total 98.8% of 13,300 collected mosquitoes were successfully identified as follows: 95.6% *Culex pipiens quinquefasciatus*, 2.7% *Aedes aegypti*, 0.35% *Anopheles stephensi*, 0.11% *Culex sitiens* and 0.05% *Anopheles dthali*. FTA cards resulted negative for the presence of RVFV.

Discussion: In this area, the Asian malaria vector An. stephensi was detected, confirming its establishment to Horn of Africa despite the vector control efforts taken over the years. Previous studies conducted in 2017 indicated *An. stephensi* as the only Anopheles in the study area. However, we here show for the first time also the presence of *An. dthali*, a secondary malaria vector, which is known to be present in Obock region, in the Northern side of the country. Large predominance of *Cx. p. quinquefasciatus* may be a consequence of insecticide resistance mechanisms in this species, considering the periodic adulticidal treatments conducted in the study area, which will be explored in further analysis. Finally, according to rare human cases reported, no RVFV was detected. However, due to the presence of potential vectors, the FTA card samples will be tested for the presence of other pathogens, particularly those transmitted by *Cx. p. quinquefasciatus* and *Ae. aegypti*, such as West Nile, Dengue, Zika and Chikungunya viruses.

ENDOTHELIAL CELLS ACTIVATION IN THE PATHOGENESIS OF COVID-19 DISEASE

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Background: Endothelial Cells (ECs) play a central role in SARS-CoV-2 infection because the endothelium is a tissue responsible for regulation of vascular tone, inflammatory responses, coagulation/fibrinolysis and maintenance of vascular homeostasis and permeability. Dysfunction of these regulated processes may directly contribute to the development of thrombotic events characterized by local vasoconstriction, ischemia of the affected organs and inflammation of the microcirculation with associated edema. The main cause of thrombotic phenomena seems to be related to cellular damage caused by either the entry of the virus and the abnormal inflammatory response of the body, which induces "cytokine storm". As a consequence, the release of pro-inflammatory cytokines by the pulmonary alveoli damaged by the virus acts at the level of the endothelium, thus causing an increase in the expression of Von Willebrand factor and adhesion molecules such as E-selectin, resulting in platelet and massive leukocyte recruitment and subsequent activation of the complement. Endothelial activation and dysfunction are suggested to be related to the coagulation cascade. Our hypothesis was that during SARS-CoV-2 infection a certain degree of endothelial activation (expressed by high level of E-selectin) occurs, and that this is more evident in patients with severe disease, i.e. those admitted to the Intensive Care Unit (ICU). Furthermore, we evaluated the possible relation between marker of endothelial activation (E-selectin) and that of coagulation (D-Dimer).

Methods: We measured plasma levels of E-selectin and D-dimer from hospitalized COVID-19 patients throughout ELISA assays. We divided patients in those admitted to ICU (n=33) and those not admitted to ICU (n=78). Association of E-selectin with clinical outcomes was also evaluated. Experiments were performed in duplicate.

Results: In ICU patients, E-selectin and D-dimer levels were significantly higher in non ICU subjects (34.89 *vs* 24.19 ng/mL and 2516 *vs* 1088 µg/mL respectively). The similar results were obtained when we observed plasma levels of E-selectin and D-dimer in patients who had developed thrombosis (n=27) compared to those without thrombotic events (n=77).

Discussion: We evaluated the degree of endothelial activation (expressed by E-selectin) and the state of hypercoagulability (expressed by D-dimer) and we found that patients with severe COVID-19 have altered endothelial and coagulation homeostasis. Vascular leakage, inflammatory reactions, coagulation imbalance and endothelial dysfunction may play a central role in the pathogenesis of severe forms of COVID-19.

USE OF BIG DATA IN PUBLIC HEALTH, A SYSTEMATIC REVIEW

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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 changing the approach to personal care, medical care and public health. In this perspective, Big Data can provide great support 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. The aim of this systematic review is to address the methodologies used to deal with Big Data in medical research, focusing on the ways in which Big Data can be effectively used in a public health perspective.

Methods: A systematic review of the literature was performed, searching in Pubmed, Scopus and Web of Science databases. Papers reporting the use of Big Data methodologies in public health will be included. The methodologies of collection, analysis and use of Big Data, as well as the challenges encountered and the strategies implemented to overcome them, will be reported. A particular interest will be placed on whether the study was guided by a hypothesis to be proved or whether a data-driven approach was used.

Results: The search retrieved 2,315 records on PubMed, 6,655 on Web of Science, and 13,020 on Scopus. After removing duplicates, 13,990 records remained, the screening of which is still ongoing. At the end of the three-year period, this doctoral project will provide concrete know-how on the possibilities of Big Data in public health, allowing their future application, highlighting the best method to be used for their analysis.

Discussion: Although the study is still in progress, the great interest around big data in medicine is evident from the number of records recovered, and the identification and understanding of the most suitable methodologies to provide good quality evidence in public health studies, is therefore crucial.

THE RELATIONSHIP BETWEEN POOR SLEEP QUALITY AND DEPRESSIVE SYMPTOMS AMONG NURSES WORKING NIGHT SHIFTS

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Background: Sleep is an active and periodic physiological state that involves the circadian clock and homeostatic process. Having enough quality sleep is important for the preservation of physical and mental health. Nurses working night shifts had worse sleep quality that negatively affect their health status. Moreover, poor sleep quality is associated with depressive symptoms.

Objective: The objective of this study is to evaluate the association between poor sleep quality and depressive symptoms among nurses working night shifts, comparing the outcomes with that of nurses working day shifts.

Methods: A total number of 244 healthy nurses will be recruited for this study. They will be assigned as follows; nurses working dayshifts (n=122) will be allocated to the control group, and nurses working night shifts (n=122) will be allocated to the treatment group. Male and female nurses between the ages of 25 to 65 years with no history of major psychiatric illness, neurological and musculoskeletal disorders and who are staff of the teaching hospital of Rome, Policlinic Umberto 1, will be enrolled for this study. Sleep quality of the nurses will be evaluated using the Pittsburgh Sleep Quality Index (Italian version), which is a commonly used 19-item psychometrically validated measure of sleep quality and disturbances. Depressive symptoms will be assessed using the Hospital Anxiety and Depressive Disorders Rating Scale (Italian version). The Independent Samples t-test will be performed to compare the means of the two groups (day-shift nurses and night-shift nurses) to determine whether there is a statistical evidence that the associated population means are significantly different. Statistical analysis will be performed using the SPSS version 25.0 (SPSS Inc., Chicago, IL, USA). Two-tailed P-values <0.05 will be considered statistically significant.

Expected results: At the end of the study, we expect that nurses with poorer sleep quality will likely show more depressive symptoms, and higher rates of depressive symptoms among nurses working night shifts will be associated with poorer sleep quality when compared to nurses working day shifts.

Future perspectives: Evidence on the association between poor sleep quality and depression among nurses working night shifts will facilitate the development of pharmaceutical agents to reduce depression and improve sleep quality caused by the disruption of the circadian clock.

THE USE OF DERMAL FILLER IN AESTHETIC MEDICINE: ISSUES CONCERNING THEIR USE, LEGAL ASPECTS AND NEED OF INFORMATION TO SHARE IN THE CURRENT PANDEMIC PERIOD

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Background: Dermal fillers have been progressively used for cosmetic procedures. Concurrently, the rates of filler complications have also increased. Among the complications, inflammatory events may occur with both hyaluronic acid and non-hyaluronic acid fillers. Evidence suggests these reactions can be immunologically triggered by viral and bacterial illness, vaccinations (i.e., influenza vaccine) and dental procedures. In the Moderna mRNA-1273 trial, three reactions were possibly related to dermal fillers out of 15,184 vaccine recipients. It is unknown how many subjects in the trial had previous treatment with dermal fillers.

Methods: My aim is to record data on SARS-CoV-2 mRNA vaccine-related reactions from soft tissue fillers in order to provide perspective for patients and practitioners regarding the incidence of reactions based on available data to date. Moreover, I will evaluate the probable disputes, which may arise from dermal filler injections during the current pandemic period.

Results: On the basis of our experience in managing dermal filler complications, I expect to collect enough data to provide information on the prevention and treatment of vaccine-related adverse events from soft tissue fillers. From the literature review, I will monitor the data and scientific literature as it develops.

Discussion: It will be possible to guide board-certified physicians in the adequate management of complications and overall, in the correct information to provide the patients before any dermal injection session. Although still very early in the vaccination process, this guidance will be meant to be helpful as we move forward during pandemic recovery efforts.

INVESTIGATING THE IMPACT OF *SCHISTOSOMA HAEMATOBIUM* INFECTION ON IMMUNITY TO *PLASMODIUM FALCIPARUM* MALARIA IN SUB-SAHARAN AFRICAN POPULATIONS

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Background: Several studies indicate that infection with helminths might modulate the immune response towards intracellular pathogens including *Plasmodium*. We recently reported that in rural villages of Burkina Faso the seroprevalence of *Strongyloides stercoralis, Wuchereria bancrofti and Schistosoma haematobium* was 5%, 16% and 63% respectively, in line with estimates of infection prevalence in the region for the three parasites. The aim of the present investigation was to assess the impact of serological markers of *S. haematobium* infection at baseline on the prospective risk of *P. falciparum* parasitaemia among study populations, using a repeated cross-sectional surveys design.

Methods: IgM and IgG against *S. haematobium* Soluble Worm Antigen Protein (SWAP) and Soluble Egg Antigen (SEA) were measured by an in-house ELISA protocol in plasma samples collected from N=452 subjects. Statistical analysis was performed using STATAv13. Descriptive analysis to assess variation in prevalence and levels of *S. haematobium*-specific antibodies according to age, sex and ethnicity was conducted using logistic and linear regression respectively. Association analysis between the presence of *S. haematobium*-specific antibodies at baseline and the number of *P. falciparum* infections measured by microscopy over 5 surveys was conducted using Poisson regression adjusting for age, sex, ethnicity and haemoglobin genotype.

Results: The frequency of subjects seropositive for both anti-SWAP and anti-SEA Ig (IgM and/or IgG) did not show differences among females and males, increased with age, and was higher in Fulani than Non-Fulani, suggesting it could be used as a marker of cumulative exposure to infection. Association analysis showed a significant increase in the incidence of *P. falciparum* infections among anti-*S. haematobium* seropositive subjects (IRR=1.30, 95%CI= 1.09-1.57, p-value= 0.004).

Discussion: Results of association analysis are in line with those of a recent systematic review and meta-analysis that suggested an association between *S. haematobium* infection and increased prevalence of *P. falciparum* asymptomatic/uncomplicated malaria. To support interpretation of these results a cohort study will be conducted in the study area to identify humoral correlates of prevalence and intensity of *S. haematobium* infection. Also, the

immunomodulatory activity of *S. haematobium* candidate proteins (H-IPSE and tetraspanins) will be investigated by testing their effect on cytokine production by Dendritic Cells *in vitro* and on the course of *P. berghei* infection *in vivo*.

DEVELOPMENT OF *IN VITRO* LUNG CELLS TO OFFER REMARKABLE NEW MODEL SYSTEMS TO STUDY MERKEL CELL POLYOMAVIRUS MOLECULAR BIOLOGY AND ONCOGENIC MECHANISMS INVOLVED IN MALIGNANCIES OTHER THAN MERKEL CELL CARCINOMA

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Background: Considering the widespread of Merkel Cell Polyomavirus (MCPyV) across the body and its strong oncogenic association with a neuroendocrine, cutaneous malignancy named Merkel Cell Carcinoma (MCC), the plausible contribution of MCPyV in tumors other than MCC cannot be ruled out. Since several studies reported the frequently detection of MCPyV DNA in healthy respiratory and cancer lung tissue, the aim of this study was to establish a pulmonary cell culture model to study the ability of MCPyV to infect and replicate in respiratory cells.

Methods: MCPyV DNA, recovered from pMCV-R17 plasmid containing the entire genome of MCPyV prototype strain, was used to transfect A549 cells, the adenocarcinomic human alveolar epithelial cells. At established time points (3-day post transfection, d.p.i. and 7 d.p.i.), cells and Supernatants (SPNTs) were collected. Viral DNA from cells was extracted, whereas SPNTs were used directly in molecular biology assays. Extracted DNA and SPNTs were quantified using qPCR targeting MCPyV small t antigen (sT). MCPyV Large T antigen (LT) and Viral Protein 1 (VP1) expression were explored by Western Blot (WB) and Immunofluorescence staining (IF).

Results: qPCR results revealed that MCPyV DNA efficiently replicated in A549 cells showing, during transfection experiments, a progressively increment of viral DNA amount from 1.5×103 copies/cell (3 d.p.t.) to 1.75×103 copies/cell (7 d.p.t.). MCPyV replication evaluated in the SPNTs, harvested at the same cell sampling times, displayed a trend of MCPyV load similar to that observed for cells. To confirm that virions were generated during the first round of transfection experiments, SPNTs collected 7 d.p.t., were used to infect freshly A549 cells. Results confirmed the same MCPyV replication trend observed during the first cycle of transfection. WB analysis showed that the LT was detected from 3 d.p.i and reaching the maximum expression 7 d.p.i. By IF at 3 d.p.i. MCPyV VP1 was not detected, probably for a delay in the whole virus assembly process. When IF was conducted 7 d.p.i, the MCPyV VP1 expression was revealed with a cytoplasmic and nuclear localization.

Discussion: This is the first study in which it has been demonstrated that A549 cells can support MCPyV infection, as confirmed by replication and LT and VP1 expression. Identify cells different to fibroblasts from the dermis supporting MCPyV infection could help to clarify MCPyV biology in respiratory system's cells and to assess the guilty or circumstantial contribution of MCPyV to lung tumor development.

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) is a rare severe gut motility disorder characterized by symptoms of intestinal mechanical obstruction in absence of lumen-occluding lesions. Intestinal bacterial overgrowth has been reported in patients with CIPO, and an improvement in pain and swelling has been reported in patients undergoing fecal microbiota transplantation. To date, many studies showed that serotonergic signalling pathways and microbiota play an important role in GI motility, but few data are available for CIPO patients. The aim of the study is to evaluate if abnormalities in serotonergic signalling, that could be triggered by alteration of the gut microbiota, are present in CIPO patients.

Methods: We aim to characterize mucosa associated gut microbiota and evaluate the expression of genes related to serotonergic pathway, i.e. serotonin synthesis (TPH1) and reuptake (SERT), in CIPO patients. We are collecting biopsies at Cesare Arrigo Hospital (Alessandria), then subjected to DNA/RNA extraction. Total DNA extracted will be used to characterize microbiota by sequencing the V3-V4 region of 16S rRNA gene. Total RNA extracted will be retro-transcribed and cDNA will be used to evaluate the expression of TPH1 and SERT genes through qPCR.

Results: To date, we have collected colon, ileum and duodenum biopsies of 7 CIPO patients and 7 controls no CIPO diagnosed (4-17 years old), maintained in All Protect Tissue Reagent at -20°C. DNA and RNA extractions were performed. After quantification DNA was used for 16S rRNA gene V3-V4 region sequencing at Biofab service. Indeed, the extracted RNA has been retro-transcribed in cDNA. Next step will be to evaluate TPH1 and SERT genes expression, and to analyze results making correlation analysis among all data. Besides, we conducted a research on literature data concerning the link between gut microbiota and ENS in subjects with intestinal motility disorders. This allowed to write a review entitled "Chronic Intestinal Pseudo-Obstruction: is there a connection with gut microbiota?" currently under review on Gut Microbes.

Discussion: Results could allow a better understanding of the mechanism by which the microbiota influences the intestinal peristalsis in CIPO patients, providing a basis to discover a possible origin of severe dysmotility. It could also represent the first step to design a new therapy targeting microbiota, improving treatment outcomes and quality of life of CIPO patients.

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 a diversity of 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. Also, Giardia duodenalis assemblages A and B, and Entamoeba species have been reported in NHP. The occurrence of zoonotic helminths has also been recorded in NHP, including *Trichuris* spp. and *Ascaris* spp. Ecosystem transformation increases contact between humans and NHP, leading to chances of zoonotic parasite transmission. Likewise, contact with captive primates can represent an occupational risk for humans leading to parasitic infections. This study aims to evaluate the prevalence and genetic diversity of intestinal parasites from NHP living in fragmented forests in Colombia, and in a wildlife recovery centre in Italy, in order to identify potentially zoonotic pathogens and explore its transmission pathways.

Methods: We collected fecal samples from free-ranging NHP *Alouatta seniculus, Ateles hybridus, Aotus griseimembra, Cebus versicolor, Saimiri cassiquiarensis*, and *Sapajus* sp. living in forest fragments in Central Colombia, as well as samples from captive macaques (Macaca tonkeana) living at Parco Faunistico Piano dell'Abatino, in Rome. Overall, 166 fecal samples were collected from different primate individuals, and faecal smears were performed in order to identify parasites based on morphology.

Results: Around 90% of the samples were positive for intestinal parasites. Protozoans (*Blastocystis* sp., Balantiididae, *Dientamoeba* sp., Entamoebidae, *Giardia* sp.), cestodes (*Hymenolepis* sp.), trematodes (*Controrchis* sp.), nematodes (Ascarididae, Trichuridae, *Strongyloides* sp., *Trypanoxyuris* sp., *Ancylostomatidae*), and acanthocephalans were found in free-ranging NHP. So far, samples positive for Ascarididae and *Blastocystis* sp. were characterized using molecular techniques, and *Ascaris lumbricoides* and *Blastocystis hominis* were identified. Captive primates were found infected with *Entamoeba* sp., *Oesophagostomum* sp., and Balantidium-like cysts.

Discussion: This study contributes new information of intestinal parasites infecting wild NHP exposed to anthropogenic disturbance. The finding of parasites with zoonotic potential suggests epidemiological implications in NHP conservation and human health, at the human-NHP interface, in transformed ecosystems. The results of this study could be useful in the design of public health policies, and within NHP conservation programs.

AMBULANCE SANIFICATION: A 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 are 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.

Methods: Analysis of scientific literature on Pubmed in the last 10 years (queries: "ambulance contamination", "ambulance personnel" and "health personnel hygiene"). Delete duplicates, not in English papers or non-relevant titles/abstract/full text.

Results: Each bacterial species always tends to colonize the same surfaces. inaccurate disinfection of ambulances and medical personnel increases the risk of colonization by Bacilli Spp. the transport of bacteria exposes patients to risk of infection, demand for greater hospital resources and antibiotic resistance. On the other hand, staff are more exposed to environmental pollution (including disinfectants) and more affected by dermatological and respiratory diseases.

Conclusion: Ambulances should be sanitized by personnel experienced in the use of sanitizers and personal protective equipment. It is advisable to reduce the duty shifts of ambulances and health personnel in order to guarantee the safety of the patients transported and of the staff.

THE IMPORTANCE OF BEING EARNEST: THE ROLE OF AUTOPSY IN PREVENTING LITIGATION RELATED TO THE MANAGEMENT OF LIVER AND DIGESTIVE DISORDERS

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Background: The management of adverse events in medicine is a major challenge for different health systems around the world. Over the years, the approach to clinical risk has seen the use of different reactive and proactive methods. In this regard, hospital legal medicine unquestionably constitutes a privileged observatory in relation to the dual activity of clinical autopsy and litigation management. Given the topicality and significance of the problem, the present study aims to demonstrate the importance of clinical autopsy in deaths following imaging, endoscopic or surgical procedures for the diagnosis and treatment of digestive and hepatic diseases. In particular, the comparison of post-mortem findings with clinical evidence will emphasize the role of clinical autopsy in identifying the suboptimal steps of care paths as well as driving the policies on quality and patient safety.

Methods: A retrospective study was conducted on 28 clinical autopsies performed between 2015 and 2021 at San Luca Hospital of Lucca and Policlinic Umberto I of Rome. All sudden unexpected deaths following procedures for the diagnosis and treatment of digestive and hepatic diseases were included. After an accurate analysis of medical records and consultation with healthcare professionals involved, all cases were subjected to autopsy and histopathological exams. The obtained data were analyzed, compared with clinical diagnoses, and shared with the risk management team to identify pitfalls and preventive strategies.

Results: Post-mortem evaluations confirmed the clinical diagnosis only in 6 cases (21.4%), presenting discordant results in the remaining 10 cases (35.7%). In the 12 cases (42.9%) in which the clinical diagnosis was labeled as "unknown" post-mortem examinations made it possible to document the cause of death.

Discussion: In reference to the accuracy of the clinical diagnosis with respect to the autopsy diagnosis, the high percentage of incongruous or unknown diagnoses can be explained by the care context; in fact, most of the examined cases were characterized by hospitalizations in emergency operating units and critical conditions upon admission such as not to allow prompt classification; in other cases the diagnostic process was limited by the inability to collect detailed anamnestic information; again, in some cases the diagnostic process was interrupted by the patient's intraprocedural death. Based on what has been proven, post-mortem examinations can concretely enrich hospital prevention systems and improve care paths. The implementation of the methodological approach outlined certainly demonstrates that, even in the risk management field, "mors gaudet succurrere vitae".

INFECTION PREVALENCE AND EPIDEMIOLOGY IN A CARDIAC SURGERY INTENSIVE CARE UNIT IN SUDAN

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Background: Antimicrobial Resistance (AMR) represents a global public health issue affecting also developing countries. In this particular setting, AMR occurrence is related to a number of factors, namely: 1) unreasonable prescription and/or self-prescription of ABT in an area with a high burden of infection diseases; 2) poor socioeconomic conditions; 3) little product regulation, oversight or quality control; 4) limited capacity for microbiology testing and lack of local and national surveillance. Infection is a major cause of morbidity and mortality in Intensive Care Units (ICUs) worldwide and cardio surgery ICU patients are particularly vulnerable. To the best of our knowledge, studies documenting the extend of AMR in Africa are sparse, particularly concerning East African countries where the surveillance capacity is rather minimal. The aim of our report is to assess the prevalence of infections and patterns of resistance in patients admitted in a cardio surgery ICU in Khartoum, Sudan (EMERGENCY NGO).

Methods: Single-center prospective study carried out from January to December 2020. In the given study period, for each patient admitted to ICU a study sheet was filled in and updated on a daily basis till patient discharge from ICU. The study sheet included a number of data: demographic, surgery, ICU staying, microbiology. Primary outcome was rate of infection in ICU and epidemiology of AMR. Secondary outcome was to identify risk factors related to primary outcome and if the incidence of infection was influencing the length of stay in ICU.

Results: A total of 611 patients were enrolled into the study. During the study period, a total of 224 Microbiological Cultures and Sensitivity (MCS) specimens were positive for infection. The distribution of infection was analyzed by site of culture (Table 3): tracheal suction (n=83; 37.0%), blood (n=55; 24.5%), CVC tip (n=35; 15.6%), urine (n=34; 15.1%), wound swabs (n=12; 5.3%), arterial line tip (n=1; 0.4%). Out of the whole study population, 15.7% (n=96) patients had at least one positive MCS culture at some point during their ICU staying. MDR epidemiology and prognostic factors analysis are still working process.

Discussion: A better knowledge of the topic might contribute to raise the awareness of the need to prevent and limit the spread of AMR and could improve clinical practice in developing counties.

MIGRANTS PEOPLE WITH DISABILITY IN EUROPE: POLICIES AND CHALLENGES

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Background: Internationally, there are 271.6 million migrants. According to the World Health Organization, about 15% of the world's population lives with a condition of disability. So, it is possible to consider with some approximation that out of 271 million migrants, 40.65 million are people with disabilities; of the 30 million people who migrate every year, 4.5 million have that condition and out of 22 million refugees, 3.3 million are refugees with disabilities. European policies on migration should consider people with disability.

Methods: Policies framework for migrants with disability in EU were searched in specific databased and critically analyzed.

Results: In September 2020, the European Commission launched New Pact on Migration and Asylum, with some controversies. The New Pact does not consider the diversity of migrants and asylum seekers with disabilities. The EU proposal for a "vulnerability assessment" does not adequately consider the rights and needs of persons with disabilities. For example, no accessible communication formats were explicitly committed. Furthermore, health and vulnerability assessments should be carried out during the pre-entry screening process. Authorities should pay "particular attention (...) to vulnerable persons, such as (...) persons with an immediately identifiable physical or mental disability". The first doubt concerns the actual ability to assess a condition of disability. In addition, asking authorities to carry out examinations on the simple observation of "immediately identifiable disability" ignores the complex needs related to disability, which we know are multiple and heterogeneous, and discriminates de facto people with disabilities. The proposed approach reintroduces a medical vision of disability and health, which is in contrast with the United Nation Convention on the Right of People with Disability and with the standards currently used at international level.

Conclusion: Member states organization are urgently called to create a network. The experiences of all the organizations, at local and national level, should be pooled to create a constructive debate able to take its proposals at the European level. Only by acting as European Community it will be possible to deconstruct a discriminatory system and guarantee respect for human rights, regardless of one's legal status, gender, disability condition or the country to which one is forced to migrate.

ANALYSIS OF CLAIMS TO PREDICT LOSS EVENTUALITY FOR HEALTH FACILITIES CONCERNING FUTURE LITIGATIONS

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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. Availability of an operational tool to attribute a definite probability of loss to each litigation before the judicial phase would be useful to increase the standardization of claims management.

Methods: We collected data along the activity of Claims Assessment Committee of a single Sapienza University Hospital. We organized existing reports in a single data warehouse using homogeneous descriptors. All the cases identified were integrated through direct consultation of paper files.

Results: We analyzed 567 different claims, over a study period of 10 years. According to patients involved, mean age was 55 (range 1-89) with no prevalence of gender. The total litigation was distributed over 47 different units; 5 wards or services accounted for 40% of claims: orthopedics and traumatology; emergency department; general surgery; neurosurgery; radiology. Course of claims was reconstructed as follows: 91 were compensated before a judicial procedure was instituted. Of the remainder, 177 cases have landed in a civil court, most of which are still pending. Compared to the claims included in the study period that progressed to the judicial stage, 29 were extinguished following a compensation payment; for 17 of them, the payment followed an explicit sentence by the judge.

Discussion: The ratio between claims for damages and the number of hospitalizations in reviewed period is 26.8. This value is higher compared to most of the series published in the literature, and the difference is even more evident considering the years with the highest incidence in the period (2012-2015). The claims settled before the civil sentence were 75%; extrajudicial payments represent less than half (48%). The number of claims resulting in compensation reflects a similar imbalance be-tween surgery and internal medicine as observed in general claims (59% against 18% of the total); the cumulative amounts, instead, are almost equally distributed between 48% of the surgical area and 41% of internal medicine. According to the published data about the distribution of health disputes, it's clear that every medical and surgical area are not generalizable because every specialty, every health service and every hospital have its peculiarities. The amount of disputes, especially the catastrophic ones, is hardly predictable.

New research topics

HEALTH DETERMINANTS IN ETHNIC MINORITIES WITH ALZHEIMER'S DISEASE AND IDENTIFICATION OF EARLY DIAGNOSIS STRATEGIES IN INDIVIDUALS WITH MILD COGNITIVE IMPAIRMENT

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Background: Alzheimer's Disease (AD) is certainly a tremendous disease burden in our society. AD is recognized as a condition that affects all ethno-cultural realities, and evidence show that people with AD is rising more rapidly in low and middle income countries where life expectancy is dramatically increasing. The steadily increase of migration flows worldwide inevitably challenges Healthcare Systems (HCS) to develop adequate support for the diagnosis, management and treatment of patients that belong to different ethno-cultural realities. Additionally, HCS should develop networks that are able to identify patients with AD from different cultures, whose perception of the disease by the patient itself and his/her family may be completely different, and understand the needs of these people by developing systems that minimize language and cultural barriers. Concurrently, the existence of biological and genetic diversities related to ethnic and sex/gender groups draw the attention to the need to implement clinical research that ensures samples much more representativeness of the real-world viewpoint. The demand of new Disease-Modifying Therapies (DMTs) in AD is stressing the need of clinical studies to assess the efficacy and safety of new investigational compounds. Monoclonal Antibodies (MABs) are getting closer to regulatory approval, however efficacy and safety data differentiated by ethnic and sex/gender groups are not available.

Objectives: Herein, we aim to characterize the issue of AD dementia among ethnic minorities with a clinical-epidemiological and public health perspective to be prepared to manage care needs of all citizens, including those who may have major issues to access to health services.

Preliminary results: Preliminary data on 22 MABs that underwent clinical studies for a total of 78 trials showed that on a total of 14,049 participants for which ethnicity was reported, 87.5% were white-caucasian, 10.4% were Asian, 1.1% were black and less than 1% were from other ethnicities.

Future perspectives: Mild Cognitive Impairment (MCI) is identified as a condition between normal cognition and AD dementia, however the identification and clinical diagnosis of MCI are facing many challenges. Early identification, particularly in MCI condition, could be critical since recent clinical trials suggest that DMTs work best if started at early stages. It is crucial to identify biomarkers that can accurately predict the progression from MCI to AD in order to start effective therapies in the early stages of the disease. Thus, in an increasingly multi-ethnic society, studies on AD should be carried out according to an external validity.

MAXI EMERGENCIES SAFETY AND HEALTH PROTECTION

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Background: The COVID 19 pandemic has severely tested traditional models for healthcare facilities. The initial difficulties faced by the National Health System negatively affected clinical and economic outcomes. Generally speaking, any catastrophic event with unknown characteristics, and which overwhelms the "normal" operational abilities, requires the development of new organizational models. These new models should enable all stakeholders to coordinate their actions and effectively meet health care demands. In the case of maxi emergencies, we must take actions to reduce public health damage, knowing however that it will be impossible to reduce the risk to zero. Those who deal in public health face a challenge that can be better tackled with a "programming" mindset. The word programming may seem far-removed from the idea of an emergency, yet in our research we aim to demonstrate that it is precisely through a forward-thinking, programming mindset that we can be prepared to face a healthcare maxi emergency and give concrete answers which will allow to protect public health. The five stages are:

1) operational strategy and strategic time management;
2) timely processing of available data;
3) creation of protected paths involving victims and operators;
4) training for operators involved in the emergency (not only for health professionals);
5) regular re-training.

In this context, we can look at Disaster management as a multidisciplinary team of experts who rapidly enact solutions for the emergency using the most accurate scientific evidence to best allocate available resources.

Objectives: The primary goal is to increase public health and safety via the development of organisational models which are flexible and can be easily amended based on the organisation's specific needs. The secondary goal is to identify/develop real-time clinical pathways able to resolve the emergency, as well as providing a protocol to manage its aftermath.

Expected Results: Developing a model that allows to plan actions to linked to planning the actions improve economics and clinicals outcomes.

Future Perspectives: Creating multidisciplinary and cross-corporate organisational systems to tackle maxi emergencies, stressing the role of prevention in disaster management.

COVID-19 PANDEMIC AND TELEMEDICINE IN LAZIO REGION: OPPORTUNITIES AND CHALLENGES FOR PRIMARY HEALTH CARE

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Background: The COVID-19 pandemic is having a considerable impact on the Italian population and the Italian National Health Service, which, in a very short time, had to reorganize itself in order to provide an appropriate response to the renewed health concerns. Indeed, because of its transmission, SARS-CoV-2 obliges to rethink the healthcare service focusing on alternative ways to provide healthcare assistance, such as telemedicine. Lazio Region, one of the 20 administrative Regions of Italy, is located in the centre of the Country, has almost 6 million inhabitants and represents one of the nation's largest economies. The Regional Health Service is organized and administered by Local Health Authorities (LHAs) and Hospitals.

Objectives: To describe and evaluate the telemedicine solutions adopted by Lazio Region and by the LHA Roma 1 and to monitor their evolution over time through questionnaires and specific activities.

Expected (or preliminary) results: The Lazio ADVICE web platform represents the regional tool used by the General Practitioners (GPs) and other Healthcare Workers (HCWs) involved in the pandemic emergency for the management of COVID-19 patients in multiple care settings. The platform also consists of a corresponding patient smartphone application called Lazio Doctor COVID in which users can insert and collect personal data and information about their healthcare status and share them with their GP and other HCWs. In the user application, patients could even complete a questionnaire that investigates COVID-19 related symptoms and epidemiologic data such as contact with a SARS-CoV-2 positive during the previous 14 days or a possible trip taken in a Country with a high incidence of new cases. A questionnaire performed at the end of 2020 among a sample of GPs of the LHA Roma 1 showed that almost 50% of GPs used Lazio ADVICE at least once, similarly to the usage data at the regional level. Moreover, they gave interesting suggestions and comments to improve the web platform feasibility.

Future perspectives: Lazio Region has adopted innovative strategies to develop an adequate response to the coronavirus pandemic, such as Lazio ADVICE. It seems that telemedicine has finally obtained the fundamental role it should have had since its institution, at least at the healthcare managerial level. The COVID-19 pandemic has accelerated the implementation of telemedicine services around the Region, starting a positive and continuous exchange of experiences, activities and best practices among all LHAs.

EVALUATION OF EPIDEMIOLOGICAL TREND AND ECONOMIC IMPACT OF REPEATED POINT-PREVALENCE STUDIES OF HEALTHCARE-ASSOCIATED INFECTIONS

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Background: Healthcare-Associated Infection (HAI) is the most frequent adverse event in healthcare settings. It is associated with increased mortality and antimicrobial resistance, leading to prolonged hospital stays and consistent financial loss for healthcare systems. Similarly, Antimicrobial Use (AMU) and Resistance (AMR) represent a growing threat to global public health and the sustainability of healthcare services.

Objectives: The objective of this study is to estimate the burden of HAIs and antimicrobial use in the Teaching Hospital Policlinic Umberto I (THPUI) of Rome describing the trend of prevalence of HAIs across the years, evaluating the economic impact and comparing data about: a) patients; b) invasive procedures; c) infections; d) prescribed antimicrobials; e) clinical setting; f) risk factors for HAIs.

Expected results: Estimation of the punctual prevalence of HAIs and evaluation of the temporal trend; stratification of results by Department/Operative Unite by type of HAI, microbial species and antibiotic-resistance profile and by class of antibiotic prescribed; identification of risk factors associated with the onset of HAI; quantification of economic impact attributable to the change in prevalence of HAIs.

Future perspectives: The methodology and related tools used in this study could be exported into other local and regional healthcare settings in order to create a standardized approach for the management of HAIs and to compare similar contexts. This could lead to implement targeted measures to prevent and control HAIs, including continuous monitoring as instrument to evaluate the effectiveness of such interventions.

A NEW TRAP PROTOTYPE FOR COLLECTING LIVE MOSQUITOES AS A POTENTIAL TOOL FOR VECTOR SURVEILLANCE

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Background: Vector-Borne Diseases (VBD) are caused over 700,000 deaths/year worldwide. One of the most important aspects of integrate management of VBD is the entomological surveillance by traps. Monitoring of mosquito and sand-fly vectors in particular are based on active aspiration traps that have the limit to maintain specimens alive for just a few hours. In these conditions, the detection of pathogens present in vectors (e.g. arbovirus) requires the cold chain for sample storage, thus limiting the trap usage in areas of difficult accessibility. Moreover, the traditional trapping approaches are unable to collect samples healthy enough to bring them in laboratory for subsequent colony setup needed for vector competence experiments.

Objectives: Purpose of this study is to design a new trap able to collect mosquitoes and sand-flies that are kept alive for more than 24 hours, avoiding the daily trap servicing and obtaining specimens in optimal health conditions.

Preliminary results: The prototype consists in a sideway suction trap that catches specimens in a collection chamber (7,5 l) at its bottom, where air circulation is allowed by a central hole. High humidity is maintained inside the trap through 7% HEC hydrogel solution. The collected specimens can feed on 10% sucrose solution placed inside the chamber. The trap design has been modified several times, reaching an optimal prototype that was tested for six replicates into a greenhouse (180x105x150 cm) in laboratory conditions. Each test was conducted for 24 hours, releasing 100-150 starved Aedes albopictus mosquitoes at each test. Preliminary results show good performances of the trap, as follows: 62% of catch median rate (5-95 percentile range: 49-73%); 99% median survival rate (5-95 range: 80-100%); 44% median feeding median rate (5-95 range: 29-58%). Additionally, two preliminary tests were also conducted on sandflies (N=40 per test) to evaluate their survival inside a collection bag under the air flow of a CDC light trap. The sandfly survival of the two tests was 65% and 73%, which was slightly low than the survival observed in a control cage (95%). This indicates that sandflies might be potentially kept in a trap under a constant air flow without major loss of specimens.

Future perspectives: Trap prototype needs further modifications to insulated collecting chamber and protect insects against sun irradiations. The trap will be tested also on sandflies in laboratory. Subsequentially, a field sampling trial is planned to evaluate its efficacy in environmental conditions.

POLYOMAVIRUS MICRORNAS CIRCULATING IN BIOLOGICAL FLUIDS DURING VIRAL PERSISTANCE

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Background: Polyomavirus JC (JCPyV) is the etiological agent of Progressive Multifocal Leukoencephalopathy (PML), a rare demyelinating disease of the brain caused by a viral lytic infection of oligodendrocytes in an immunocompromised setting. Over the past few years, PML has been increasingly diagnosed in patients treated with immunomodulatory therapy, such as natalizumab in Multiple Sclerosis (MS) patients. Although JCPyV has been extensively studied, the risk factors of JCPyV reactivation remain elusive. JCPyV is a circular non-enveloped double strand DNA virus, with a relatively small genome (about 5000 bp). Its genome is organized in two different regions of similar size, known as early and late transcript units. These units are divided by a Non-Coding Control Region (NCCR) containing the origin of DNA replication (ori), the TATA box, cellular transcription factors binding sites and enhancer elements for the transcription of early and late genes. Recently, it was demonstrated that JCPyV encodes two mature microRNAs (miRNAs), JC-miRNA-3p and -5p, that can down-regulate early viral expression and are likely involved in the regulation of viral persistence and in the evasion of immune response. Interestingly, a recent study showed that this miR-J1-5p can be detected in biological samples of JCPyV-seropositive and of JCPyV-seronegative immunosuppresed individuals, thus indicating that miR-J1-5p could be a biomarker of JCPyV infection more sensitive than serology.

Objectives: In order to assess their potential role in counteracting viral replication to maintain its asymptomatic status in the host, we will investigate the presence of JC-miRNA-3p and -5p extracted from exosomes directly from urine and peripheral blood samples obtained from MS patients during Ocrelizumab therapy.

Expected results: Our results will give us an insight into what is happening in MS patients treated with ocrelizumab. Monitoring changes in the expression of the JCPyV miRNA may be to help in the clarification of the early virus reactivation mechanism and of clinical relevance in identifying patients at risk of PML.

Future perspective: To evaluate the biological role of miR-J1-5p and miR-J1-3p in viral replication control could be necessary to set-up an *in vitro* model. Observing the miRNAs expression is important to develop a more effective therapeutic strategy. Analyses of miRNAs expression in model of *in vitro* infection could be important in diseases, like MS, in which the virus is a risk factor for particular drug treatments, as they would help the clinician in determining the best pharmacological and rehabilitative strategy.

EPIDEMIOLOGY, RISK FACTORS AND PATHOGENETIC IMPLICATIONS IN NOSOCOMIAL BLOOSTREAM INFECTIONS

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Background: In the last 10 years the epidemiology and risk factors of Bloodstream Infections (BSI) have changed. Increasing use of medical technology and devices, the availability of life-saving treatments such as immunosuppressive drugs, solid organ and hematopoietic stem cell transplantation, and improved intensive and supportive care have allowed for the survival of more severely ill patients, patients who are extremely vulnerable to infection. Several important interventions, including adherence to guidelines on insertion and care of CVCs, use of antimicrobial or antiseptic impregnated catheters, and improved compliance with hand hygiene are necessary to reduce the risk of BSI. BSI impose an antimicrobial treatment, but the emergence of Multidrug-Resistant (MDR) pathogens determined reduction of treatment choices and, consequently, higher hospital mortality. It is known that Clostridioides Difficile Infection (CDI) and CP-CRE (Carbapenemase-Producing Carbapenem Resistant Enterobacterales) intestinal colonization represent conditions at high risk of development of nosocomial BSI caused by Candida spp. or other enteric bacteria. Also, in critically ill patients, the development of a systemic inflammatory response related to surgery, ischemia-reperfusion syndrome after major surgeries, and the use of extracorporeal circulation, all conditions related to a lower rate of intestinal perfusion, have been associated with a microbial translocation and might be involved in the pathogenesis of infective and non-infective conditions.

Objectives: The main objective of this research is to analyze prevalence, risk factors and clinical and pathogenetic implications in nosocomial BSI in different scenarios such as before, during and after COVID-19 pandemic. Secondary objective is to assess when microbial translocation could be a risk factor for BSI caused by intestinal pathogens.

Expected results: We expect to demonstrate that the damage of intestinal mucosa, caused by CDI, CP-CRE or other intestinal inflammatory conditions including SARS-CoV-2 infection of the gut, possess a pivotal role in the pathogenesis of BSI caused by enteric bacterial and fungal pathogens.

Future perspectives: Knowing prevalence and risk factors of nosocomial BSI as well the pathogenetic mechanisms underlying gut damage during several infective conditions may contribute to find strategies aiming at reducing BSI caused by intestinal pathogens.

DEVELOPMENT OF MOLECULAR ASSAYS ON PLASMODIUM GAMETOCYTES FOR FUNCTIONAL ANALYSIS AND NOVEL DIAGNOSTICS ON MALARIA PARASITE TRANSMISSION

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Background: Five parasite species of the genus Plasmodium are responsible of the malaria disease. New tools and strategies and the improvement of existing interventions are needed to eliminate malaria. Transmission blocking interventions and entomological surveillance constitute the most promising approaches. Transmission blocking interventions target gametocytes, the sexual stages of the malarial parasite circulating in human peripheral blood, responsible for parasite transmission from the human host to the mosquito vector. Monitoring tools to better understand the spread and distribution of the malaria parasite and prevent the development of new foci of infection are important for efficient transmission control.

Objectives: The first aim of this work is to use real time PCR assays, based on detection and amplification of gametocyte- and sex-specific transcripts to estimate gametocyte presence and sex-ratio in human infected blood and to estimate infectivity of individuals to mosquitoes. These assays can be used to test the activity of compounds inhibiting the viability of gametocytes or the development of the subsequent mosquito parasite stages in the insect vector. The second aim is to develop molecular assays to identify the presence of Plasmodium in Anopheles mosquitoes collected in the field and to develop multiplex assays to identify coinfections of different parasite species. The third aim is to evaluate the vectorial competence of autochthonous mosquitoes by characterizing the transmissibility and infectious charge of Plasmodium in Italian Anopheles mosquito species in experimental infections.

Expected results: Establishment of real time PCR assays (TaqMan) protocols based on amplification of sexual stage specific transcripts: pfs25 to detect and measure gametocyte presence, and pfCCp4 and pfMGET to measure the gametocyte sex ratio. Use the assays to test new generations of compounds that block transmission by killing gametocytes or influencing their development. Development of molecular assays to detect parasite presence in infected Anopheles mosquitoes. These assays will be developed by producing mixes of insect and P. falciparum extracts, in view of the possibility to conduct P. falciparum experimental infections in mosquitoes for validation.

Future perspectives: Use the assays to screen candidate compounds for their activity against gametocytes. Use sex specific assays to understand the influence of the sex ratio and its perturbations by drug treatment on parasite transmissibility in mosquitoes. Use new diagnostic tools on Italian Anopheles mosquitoes to measure vectorial capacity and to identify vectors of malarial parasites in surveillance activities in Italy or in endemic countries.

COMPARATIVE IMMUNOHISTOCHEMICAL AND MOLECULAR BIOLOGY STUDY IN DATING TRAUMATIC BRAIN INJURY (TBI)

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Background: Traumatic Brain Injury (TBI) is the third leading cause of mortality worldwide. It occurs as a result of sudden acceleration or deceleration within the skull or from a complex combination of movements and a sudden impact. TBI has been the subject of clinical, radiological, histological and immunohistochemical studies: the central issue remains the dating of brain damage and its temporal location. Molecular biology has produced promising results. By studying micro RNAs, segments of non-coding RNA involved in the regulation of gene expression, information was provided on the correlation between the expression of miRNAs and the time elapsed since the head injury. Also immunohistochemical studies revealed increased expression of molecules as Peripherin (PRPH), Calsenilin (CSEN), indicating their potential as biomarkers of early TBI.

Objectives: The objectives are to perform a comparative study between immunohistochemistry and molecular biology to assess the sensitivity and specificity of these techniques in dating early TBI, and to identify a panel of miRNAs regulating and involved in the processes of TBI (miR-21, miR-27a, miR-107 and miR-155), in order to recognize specific miRNAs for the dating of the damage as diagnostic tool in forensic pathology. In addition, the three antibodies anti-PRPH, anti-CSEN and anti-FLIP will be tested to provide information on the mechanisms of TBI in humans, to provide reference data for the diagnosis of DAI to improve the post-mortem diagnostic rate of early TBI. We aim, through the combined use of immunohistochemistry and miRNAs, to arrive at a method that allows for scientifically appropriate dating of TBI.

Expected results: At the end of the research, it will be assessed whether the newly selected immunohistochemical markers do meet the qualitative and quantitative criteria for a scientifically reliable and reproducible diagnosis of the timing of TBI. Furthermore, after evaluation of the expressivity of the miRNAs tested, it will be determined whether they can be used for the diagnosis and timing of TBI lesion viability, thus enabling their use in forensic pathology. We will evaluate the usefulness and reliability of the new immunohistochemical markers in the diagnosis of TBI and we will assess whether the miRNAs tested can be useful in the diagnosis and in the timing of TBI, allowing a possible use in forensic and clinical settings.

Future perspective: The qualitative and quantitative study of miRNAs provides information on their role in cell function, both in physiological and pathological states. Forensic pathology could benefit from the use of molecular biology: indeed, there are numerous cases in which forensic investigation doesn't lead to a definite diagnosis.

ASSESSMENT OF THE ECOTOXICITY INDUCED BY VETERINARY PHARMACEUTICALS AND THEIR MIXTURES IN THE AQUATIC VERTEBRATE DANIO RERIO THROUGH A ONE HEALTH APPROACH

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Background: The release of chemicals in the aquatic environment as a result of many different human activities is one of the major challenges of the last decades. Thousands of different compounds (frequently in small doses or mixtures) can be found in different water bodies where they pose a threat to human and environmental health. Among these compounds veterinary pharmaceuticals are frequently found, given their frequent use and their tendency to be only partially absorbed by the treated animal.

Objectives: The aim of this project is to evaluate the effects derived from the exposure to recently developed veterinary pharmaceuticals in the aquatic vertebrate Danio rerio. In order to obtain a more comprehensive picture on the matter, compounds with similar structures will be tested both individually and in mixtures. To highlight the mode of action of the examined substances both lethal and sublethal endpoints will be considered. Of particular interest will be the presence of neurotoxicity and abnormal behaviour.

Expected results: The results of this study will be useful to broaden the already existing knowledge about the effects that this class of compounds can have on the ecosystem, through the use of a well-known and widely used model organism such as Danio rerio. Moreover, by using mixtures of chemicals, synergistic effects not always detectable with chemical analysis may be observed.

Future perspectives: The data obtained from this study will be helpful in the process of drafting new guidelines aimed to regulate the release on the market of newly developed veterinary products. Also, it will help to better understand how the release of mixtures of chemicals in the environment may affect the trophic chain and may pose a threat to human health.

PROFILES OF MEDICAL PROFESSIONAL LIABILITY IN THE COVID-19 EMERGENCY. PROSPECTIVE ANALYSIS OF REGULATORY DEVELOPMENTS AND JURISPRUDENTIAL GUIDELINES

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Background: The COVID-19 pandemic of the year 2020, constituting a medical emergency of an exceptional and extraordinary nature, has had important health, social and economic repercussions within national and supranational systems, as in the field of professional medical liability.

Objectives: The objectives of the project are therefore to assess whether, in the context of the emergency pandemic of COVID-19, it is necessary to update the legislation on medical professional liability. In this regard it will be necessary to analyse the professional responsibility profiles of both the health professional and the structure.

Expected results: It is expected to obtain clarification on the position of the case law in matters of special difficulty (art. 2236 cc), of the state of necessity, of the shortage of places in intensive care, of the responsibility for nosocomial infection, of the responsibility of healthcare worker, of the responsibility of the facility.

Future perspectives: The dramatic situation created by the COVID-19 pandemic has led to direct proposals for changes to the rules governing medical liability, also at the direct solicitation of the health professionals engaged in the first line in the emergency. In Italy, some amendments to the Decree-Law March 17, 2020, n. 18 c.d. "Cura Italia" moved in this direction. The multiplicity of the amendments proposed by the politicians indicates the interest in solving a contemporary legal problem that needs answers from the institutions.

INTESTINAL DAMAGE AND MICROBIAL TRASLOCATION DURING CORONAVIRUS DISEASE-19: CLINICAL AND PATHOGENETIC IMPLICATIONS

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Background: Intestinal involvement during COVID-19 is not uncommon and is mainly explained by the presence of ACE-2 receptors in intestinal cells. In fact, recent studies have shown that up to one-third of COVID-19 patients also experience gastrointestinal symptoms such as diarrhoea and vomiting, that leave thinking that a certain degree of gut involvement during the course of infection may occur. Intestinal damage following COVID-19 infection may lead to microbial translocation, i.e. the migration of bacteria or their products from the intestine to the extraintestinal space and possibly to the systemic circulation.

Objectives: The main aims of this research are to analyze markers of intestinal damage (fatty acid binding protein 2 or FABP2) to check the presence and degree of alteration of intestinal cells integrity during the course of COVID-19 infection and to analyze the levels of LBP (Lipopolysacharide Binding Protein) and EndoCab IgM, both markers of microbial translocation. An additional hypothesis is that the degree of microbial translocation may play a role in the development of Bloodstream Infection (BSI) after COVID-19.

Expected results: We expect that during SARS-CoV-2 infection there is a degree of intestinal damage and disruption of the intestinal mucosa that may be responsible for the subsequent development of systemic infections caused by intestinal microorganisms. In particular, we expect that patients with COVID-19 have elevated levels of intestinal damage compared to healthy controls and that these are maintained during the course of infection, and that patients with severe COVID-19 admitted to the intensive care unit have higher degree of microbial translocation.

Future perspectives: Should COVID-19 be associated with persistent intestinal permeability and intestinal damage, strategies targeting at reducing both these conditions may be considered to reduce the severity of infection.

COMPARATIVE STUDY BETWEEN CONVENTIONAL AND NEW METHODS IN DEFINING THE CAUSE OF DEATH FROM ANAPHYLACTIC SHOCK

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Background: Anaphylaxis is defined as a rapid systemic reaction that develops in individuals previously exposed to specific allergens, which lead to specific IgE production, binded to membrane receptors in mast cell and basophils. On second exposure to the allergen, it binds to the IgE antibodies on the surface of the mast cells and basophils, leading to degranulation of the cells and release of primary and secondary mediators, which in turn leads to cardiovascular and respiratory changes that are fatal if not treated immediately. The determination of a correct post-mortem diagnosis is problematic in forensic cases. Traditional methods, such as histopathological examination of the respiratory tract and the use of specific antibodies used in immunohistochemistry, like anti-tryptase antibody and anti-CD117, are sensitive but not always specific and therefore do not guarantee a high degree of probability in the diagnosis of anaphylaxis. Also biochemical techniques are used, like tryptase assay in femoral blood and urinary samples. However, these approaches represent only an excellent aid for the diagnosis of anaphylactic death, but in forensic practice it is necessary to reach a certain diagnosis in probabilistic terms. For this reason, molecular biology, in particular miRNA, has provided promising results in recent years, which can provide important information. Numerous pathological and physiological processes, such as cell cycle, cell metabolism and immune response are regulated by miRNAs.

Objectives: Aim of this study is to compare immunohistochemical technique with molecular biology one to obtain a reliable diagnosis of anaphylactic death in probabilistic terms. For the immunohistochemical study, trachea and lung samples will be analyzed. A miRNA panel involved in cell activation and consequent anaphylaxis (miR-21, miR- 27a, miR-107 and miR-155) will be located in trachea and lung samples. Moreover, also blood samples will be analyzed for the quantitative toxicological assay of tryptases and miRNA.

Expected results: At the end of this study, new marker will be identified, like miRNA and immunohistochemical one. The use of new selected immunohistochemicals markers, as already present in the literature, meet qualitative criteria and quantities useful to allow a scientifically reliable diagnosis of the diagnosis of anaphylactic death, thus allowing its use in a pathological-forensic context.

Future perspectives: From the discovery of regulatory role of miRNA, it is possible to study their role as potential biomarkers and therapeutic targets in many pathological conditions, opening new frontiers of research, like anaphylactic death.

PAIN THERAPY IN ALBANIA, A DESCRIPTIVE RESEARCH AIMING TO HIGHLIGHT THE RIGHT MEANS FROM ANCIENT TILL MODERN, TOWARDS A PAIN-FREE PATIENT

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Background: Pain is one of the main reasons a patient goes to a doctor and one of the main expectations from a doctor is to relieve/stop the pain. Humans used to calm pain for thousands of years, with what we nowadays refer to as alternative medicine. Since the first analgesic drug was first produced, around year 1800, the huge progress in medical sciences and technology as well as the formation of Pain Management as a field of medicine, around year 1960, Pain Therapy did reach highest achievements ever in human history. Nevertheless, there are ancient treasures that need to be promoted simultaneously with modern developments regarding Pain Management as a basic medical competence. Considering the huge mental and spiritual health impact of painful experiences in human life and the fact that there can't be complete health without mental and spiritual health therefore digging deeper in global knowledge and promoting the best of it globally it's a human right and divine mission.

Objectives: Help medical staff in Albania reset their focus on pain and the right of the patient to live and/or die with dignity. Introduce Pain Management's protocols, techniques and Physical Therapy modalities. I see this as a precious step towards a better understanding of Pain Therapy from medical staff and therefore offering the best available solutions to our patients.

Expected results: Based on preliminary observations I expect that data will demonstrate lack of information and clinical skills about Pain Therapy in developing countries like Albania, lack of appropriate medical staff who would be capable to evaluate and manage pain properly, lack of psychological support to the patient in pain, lack of financial support towards pain free hospitals as well as lack of updated protocols about pain management in Albania.

Future perspectives: A better understanding of what pain is and its components, including pain therapy in studying programs in developing countries, mastering ancient ''alternative'' remedies and techniques which alleviate/ stop pain along with modern inventions will make possible a huge practical improvement in Pain Management, will decrease abuse and wrong use of analgesics worldwide, will improve outcomes in chronic pain patients and offer to everyone who prefers it, a pill-free cure for pain.

SEVERE COVID-19 AND INVASIVE PULMONARY ASPERGILLOSIS CO-INFECTION IN PATIENTS ADMITTED IN SUB-INTENSIVE CARE UNIT: CLINICAL FEATURES, RISK FACTORS AND OUTCOMES

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Background: Viral pneumonia increases susceptibility to bacterial and fungal superinfections, including Invasive Pulmonary Aspergillosis (IPA). IPA is an emerging secondary infection in patients with COVID-19, especially in Intensive Care Unit (ICU). Several reports described the COVID-19 Associated Pulmonary Aspergillosis (CAPA) indicating excess mortality rates compared with patients without evidence for aspergillosis. CAPA develops even in absence of classic host factors for IPA, and it is unknown whether SARS-CoV-2 represents itself a risk factor for IPA or whether additional risk factors are involved, such as lymphopenia and corticosteroid therapy. Diagnosis is insidious, especially in patient with COVID-19 and acute respiratory distress syndrome, considering that many radiological signs of COVID-19 pneumonia can mimic IPA. Microbiological analyses of respiratory samples and detection of galactomannan can aid to diagnose CAPA in patients presenting worsening respiratory failure or haemoptysis. Therefore, prompt diagnosis of IPA in COVID-19 and antimycotic therapy administration can play essential role. To our knowledge, most data refer to patients admitted to ICU, whereas little is known about CAPA in patients admitted to sub-intensive care unit.

Objectives and preliminary results: Our study aims to evaluate the incidence, risk factors, clinical course and outcomes of CAPA in COVID-19 patients admitted to the respiratory sub-intensive unit of Policlinic Umberto I, Rome. From September 2020 to May 2021, we observed 578 COVID-19 patients presenting with severe respiratory failure and treated with non-invasive mechanical ventilation. Median age was 71 years (25-92). Comorbidities were mainly respiratory disease, diabetes and cardiovascular diseases. All patients required a corticosteroid course treatment and presented with different degrees of lymphopenia. Overall, six cases of CAPA (1%) were diagnosed according to both clinical suspicion and international guidelines for IPA in patient presented worsening respiratory failure or haemoptysis without evidence of bacterial superinfections. Despite prompt isavuconazole treatment, mortality was high (4/6, 66.7%).

Future perspectives: Our study suggests that CAPA is an emerging challenge also in sub-intensive care units. It could explain common features or differences between patients admitted in ICU or in sub-intensive care units. Moreover, considering the high mortality of CAPA in severe COVID-19 patients, this study could also determine if there are some indications to prophylactic treatment with isavuconazole in patient at high risk for CAPA.

IMMUNOLOGICAL EFFECTS OF OLT1177 ON PBMC PRODUCTION OF PRO-INFLAMMATORY CYTOKINES AMONG PEOPLE LIVING WITH HIV

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Background: Even in condition of viremic suppression under Antiretroviral Therapy (ART), People Living With HIV-1 infection (PLWH) show chronic immune activation/hyper-inflammation inducing the premature onset of HIV-related non-AIDS-defining comorbidities. Compared to healthy controls, higher concentrations of IL1β and IL18 can be detected in PLWH with cardiovascular and/or neurocognitive disease. OLT1177 is small synthetic molecule, which targets specifically the NLRP3 inflammasome and prevents the activation of caspase-1 and the maturation and release of IL-1β and IL18 from NLRP3 inflammasome expressing cells, such as Peripheral Blood Mononuclear Cells (PBMC). OLT1177 has been shown to be well tolerated in humans is currently in clinical studies for the treatment of inflammatory conditions, available as oral capsule dosage formulation. It also ameliorates clinical and histological phenotype of Alzheimer's disease mouse model.

Objectives: The main objective is to show that ex vivo OLT1177 reduces IL1β and IL18 production by PBMC of PLWH under virologic control and optimal compliance to ART but affected by cardiovascular and/or neurocognitive disease. To do that, PBMC will be isolated from PLWH and divided in two groups, one receiving and other not receiving pre-treatment with OLT1177; subsequently, PBMC will be cultured with antigenic stimuli of different nature (bacterial, viral, fungal) for 24 hours and lastly pro- and anti-inflammatory cytokines (including IL-1β and IL18) will be measured in the supernatant. Secondary objectives of the study are to measure blood levels of pro - and anti-inflammatory cytokines as well as of intestinal translocation markers, to check their association with biological response to OLT1177 ex vivo, and ultimately to define a clinical inflammatory/translocation cut-off to detect PLWH who could benefit from treatment with OLT1177.

Expected results: We expect to show a significant reduction of IL1β and IL18 concentration in the supernatant of PBMC treated with OLT1177 compared to the supernatant of PBMC treated with placebo, after antigenic stimulation ex vivo.

Future perspectives: If the expected results will be satisfied, a clinical trial to assess the efficacy of OLT1177 in decreasing *in vivo* the chronically high levels of IL-1β and IL18 detected among PLWH would be the natural perspective of the current study: this would allow to study the clinical efficacy of OLT1177 in diminishing the physiopathological component underlaying the HIV-1-related non-AIDS-defining comorbidities, with focus on cardiovascular and neurocognitive disorders.

DELIVERY OF BIOACTIVE SUBSTANCES WITH ANTI-PROLIFERATIVE AND ANTIMICROBIAL ACTIVITIES BY NANOEMULSIONS FORMULATED WITH ESSENTIAL OILS

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Background: Phytochemicals are naturally occurring bioactive compounds found in vegetables, fruits, spices, and other plant foods. Resveratrol (RV), a polyphenol non-flavonoid compound present in strongly pigmented vegetables and fresh fruits as well as dried nuts, exhibits diverse biological activities such as antitumor, antioxidant, cardio- and neuro-protective and anti-aging. RV appears to inhibit cell growth, induce cell cycle arrest and apoptosis in various cancer cell lines via several signaling pathways. RV also has a strong antibacterial action by interfering with the mechanisms related to the biofilm formation capacity, the motility, adhesion and expression of flagella. A potential use of RV against persistent infections has recently been suggested. Due to the low bioavailability, rapid metabolism and photosensitivity, the use of RV in the pharmaceutical field is difficult. Recently, the use of nanotechnology to enhance delivery of phytochemicals has received considerable attention. A fascinating strategy is represented by Nanoemulsions (NEs), emulsions with a particle diameter in the nanometer scale consisting of an internal oil phase finely dispersed in the form of droplets in a continuous aqueous phase thanks to the action of non-ionic surfactants. An advantage of these formulations is the flexibility that can be exploited in the design. A variety of plant-derived Essential Oils (EOs), characterized by an intrinsic pharmacological effect, can be used to prepare NEs and lipophilic compounds can be incorporated in their hydrophobic core.

Objectives: The present study aims to formulate and characterize new NEs as tools for improving delivery and intracellular concentration of natural bioactive compounds, such as RV. The changes in cell cycle progression, induction of apoptosis, activation of the autophagy machinery in cancer cell lines of different origin, the antimicrobial activity towards clinical multidrug resistant bacteria and the influence in the invasive ability of persistent bacteria of RV free or loaded in NEs will be assayed.

Expected results: The possibility to modulate the composition and dimensions of NEs is particularly useful to obtain the suitable vectors for a specific application. We expected that the use of different combinations of EOs and surfactants, will permit the development of new delivery NEs able to improve, through a synergistic action, RV bioactive characteristics.

Future Prospective: NEs constitute one of the most promising system for delivering and improving the bioavailability of bioactive compounds. New designed NEs loaded with RV from this study could be represent a starting point to evaluate this tool in *in vivo* studies or clinical applications.

ONE HEALTH STRATEGIES: STRENGTHENING PREVENTION AND PREPAREDNESS HEALTH SYSTEMS

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Background: One Health (OH) is an approach to global health security that recommends a holistic view of health and health related events occurring at human, animal and ecosystem interface. It promotes an interdisciplinary, intersectoral perspective to disease emergence and control and its strategies can be adopted by policies and legislation and implemented in research and programmes to achieve better public health outcomes. OH approaches are implemented to enhance the surveillance and control of arbovirus infections in the MediLabSecure Network (Mediterranean, Black Sea and Sahel Regions).

Objectives: The general objective is to contribute to the strengthening of prevention and preparedness plans with the integration of One Health Strategies. For what concern the specific objectives, they are:

- to collect, analyse and describe the information about the exchange of data, and how it is organised, of the sectors involved in the surveillance of arbovirus infections (including relevant environmental data) in three countries of MediLabSecure Network and to understand how this information can improve early warning and risk assessment with a One Health approach;
- to analyse OH strategies that have been implemented to improve and enhance prevention and preparedness to epidemics and pandemics.

Expected results: Recommendations on strategies and actions to improve prevention and control of viral infections.

Future perspectives: Contribution to the implementation of harmonised surveillance and preparedness strategies in the Regions with a One Health approach.

VIRUS INFECTION IN THE BRAIN AND COMPLEMENT ACTIVATION: POSSIBLE ROLE IN NEURODEGENERATION?

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Background: Different viruses including Herpes Simplex Virus type 1 (HSV-1) and respiratory viruses such as influenza virus and SARS-CoV-2 can reach the Central Nervous System (CNS). A growing body of experimental and epidemiologic data point to viral infections as possible risk factors for neurodegenerative diseases, including Alzheimer's disease. The host immune responses and the activation of inflammatory processes cause chronic damage resulting in alterations of neuronal function and viability, but different pathogens can also directly trigger neurotoxic pathways. Among the host defence, the complement system bridges innate and adaptive immunity against microbial infection and its aberrant activation may play a role in virus-induced damages.

Objectives: Focusing on viruses able to reach the brain, we will firstly analyse whether primary infection or reactivation of a latent virus can cause an increase in expression or activation of complement proteins. Then, we will explore whether this increased activation of complement leads to an augmentation of complement-dependent neuronal pruning and if this phenomenon is correlated to cognitive deficits.

Expected results: By studying the complement cascade activation upon brain virus infection and its role in neurodegeneration, we will shed light on the role of the host/virus relationship in determining damages in the brain.

Future perspectives: Understanding whether viral infections cause neural damage in a complement-dependent manner can help us in the understanding of the molecular mechanisms leading to neurodegeneration. This knowledge may be useful for the development of possible novel therapeutic approaches.

SIMULTANEOUS DETERMINATION OF ORGANIC GUNSHOT RESIDUES AND STABILIZERS IN ORAL FLUID BY MEANS OF UHPLC-HESI-HRMS ANALYSIS

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Background: In recent years, due to the increasing use of lead-free and heavy metal ammunition, forensic science has shown a growing interest in the detection of Organic Gunshot Residue (OGSR). Identifying traces of explosives on individuals, clothing, homes and cars and other related objects is intended to determine if contact with explosives has occurred. Since contact could indicate illegal possession or handling of explosives or possible involvement in a shooting, it is important that the identification of explosives on suspects is highly reliable.

Objectives: The purpose of this work is to create a method for the determination of the most common explosives and the most used stabilizers, coming from both firearms residues and post-deflagration in forensic samples (biological matrices, surfaces etc.).

Preliminary results: A method has been developed in which it is possible to simultaneously determine some of the most common explosives, as well as OGSRs, and the most common stabilizers, in the oral fluid matrix, in a single chromatographic run.

Future perspectives: Our studies have the dual purpose of finding traces of explosives both for forensic purposes in the hypothesis of a crime with a firearm or exposure to explosives in the case of packaging bombs, and for medical purposes in the prevention of symptoms as well as damage due to exposure to explosives (also considering the approach of minors to the competitive sport of skeet shooting and dynamic shooting). The possible exposure of people who do not use explosives but who frequent indoor and outdoor shooting ranges will also be addressed, also evaluating any resulting environmental pollution levels, and then evaluating simple passive exposure.

VACCINACTION: EDUCATIONAL STRATEGIES AS AN ANSWER TO NEW PUBLIC HEALTH CHALLENGES IN THE FIGHT AGAINST VACCINE HESITANCY

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Background: In 2019, the World Health Organization (WHO) declared Vaccine Hesitancy (VH) as one of ten major global health threats. VH also involves Healthcare Workers (HWs), who play a central role in explaining vaccine benefits and risks, recommending vaccines, and vaccinating the community. Inadequate knowledge and lack of confidence in the efficacy and safety of vaccines seem to be the main determinants of VH in HWs. VH is already encountered in HWs during university training, especially in nurses, defined by the WHO as one of the most influential figures for the immunization programs. The SAGE Working Group on VH suggests enhancing nursing students' knowledge and communication skills to enhance the community adherence of vaccination programs.

Objectives: The aim of the research project is to design and implement a standard educational program for the enhancement of knowledge, attitudes, intentions to vaccinate and communication skills related to immunization programs and strategies against VH in nursing students of Sapienza University of Rome. In order to achieve the primary outcome, three project phases have been defined: i) Identify measurement tools, intervention strategies and VH determinants in HWs through a systematic review of literature; ii) Identify the training needs of nursing students regarding knowledge, attitudes and intentions to vaccinate through analysis of educational curricula, cross-sectional studies and Skill Labs concerning the nursing students classes enrolled in the first year; iii) Design, program and evaluate the impact of an educational intervention.

Preliminary results: A systematic literature review is being conducted on PubMed, Scopus, CINAHL, Web of Science, Cochrane, Joanna Briggs Database, and ERIC. The search protocol was registered on PROSPERO (ID: CRD42020212252). Of the 7724 articles identified, 4531 were included after the removal of duplicates. 2255 were considered eligible after screening titles. At the end of the synthesis process: i) a validated diagnostic questionnaire will be selected for the evaluation of the communication skills of knowledge, vaccination intentions in nursing students; ii) the most effective educational tools will be synthesized; iii) VH determinants associated with healthcare professionals will be identified. Finally, it will be possible to carry out a standardized educational intervention on the basis of educational needs.

Future perspectives: The synthesis of evidence for VH in HWs and the implementation of an educational intervention for nursing students could lead to health policy benefits by producing strategies and recommendations aimed at increasing vaccination adherence among HWs and general population.

AN ORGANOTYPIC MODEL FOR THE STUDY OF RETINAL *T. GONDII* INFECTION

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Background: Histopathology information of active Ocular Toxoplasmosis (OT) lesions in humans is difficult to gather, the majority of information about the inflammatory response and the morphological changes can be based on a murine model of Congenital OT (COT).

Objectives: With the present study we aim to create an *ex vivo* model that facilitates the observation and manipulation of the infected retina. The first objectives are: to stabilize the murine retinal ex-plants, to establish a dose-dependency for *Toxoplasma* infection and to define the incubation time(s). Once the model is defined, we will start observing changes produced during *T. gondii* infection.

Expected results: The primary result we expect is to optimize an organotypic model of retinal *Toxoplasma* infection that will allow us to observe the course of infection, at different times. Not only retinal tissue changes will be observed, but also the possible cell preferences by the parasite, the inflammatory response, the oxidative stress, or the cell death mechanisms (necrosis, apoptosis, necroptosis, autophagy).

Future perspectives: Once the model is settled, its manipulation could shed light on possible treatments, especially for immunocompromised hosts.

CONCOMITANT MEDICATION POLYPHARMACY, INTERACTIONS AND OVER THE COUNTER MEDICAMENT IN A COHORT OF HIV ELDERLY PATIENTS

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Background: Advances in Antiretroviral Treatment (ART) over the past 30 years have significantly prolonged the life expectancy of People Living With HIV (PLWH), whose median age has progressively increased. Thus, as they may experience a prematurely aging than general population, PLWH require more medications to treat comorbidities in addition to ART. The increasing complexity of therapeutic regimens may have a negative impact on the quality of life, adherence to treatment and inevitably increases the chance of drug–drug interactions that may lead to unintended adverse events.

Objectives: This is a multicentre, cross-sectional study to investigate potential interactions between ART and non-ARV medication in an Italian cohort of older PLWH. Further objectives are to investigate potential interaction among non-ARV medication, and the prevalence of over the counter and non-conventional medication and their possible interactions with ARV drugs.

Preliminary results: First data shows that the use of nucleoside reverse transcriptase inhibitor + integrase strand transfer inhibitor rather than nucleoside reverse transcriptase inhibitor + nonnucleoside reverse transcriptase inhibitor and protease inhibitor–based regimens was associated with a reduced risk of potential drug-drug interaction. The use of non-conventional medication has been found in a half of the patients, with a high proportion (45%) of potential interaction with ART.

Perspectives: Complete the cohort will give a national view of actual harm caused by polypharmacy in PLWH, and develop optimal strategies to facilitate and promote the effective and safe use of medication.

CITIZEN SCIENCE APPROACHES FOR INCREASING KNOWLEDGE ON MOSQUITOES AND REASING AWARENESS ON MOSQUITO BORNE DISEASES IN ITALY

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Background: The risk of exotic mosquito-borne disease transmission is increasing in Italy due to environmental and sociological changes, which in the last decades have increased the risk of importation of human infected cases, as well as allowed the invasion and colonization of temperate regions by tropical mosquito vectors (e.g. Aedes invasive species). In the absence of vaccines for most mosquito-borne diseases, the possibility to decrease the risk of transmission lies on the prevention of the invasion by novel vector species and on the control of their densities in already colonized countries. Both goals imply a good knowledge of the phenomenon and of the containment strategies by the public health personnel, as well as by citizens.

Objectives: The objective of the thesis project is to contribute to Citizen Science activities ongoing in the Medical Entomology group (e.g. MosquitoAlert project and #scattalazanzara 2021-social media campaign) by identify and develop science communication strategies finalised to engage the civil society, raise awareness on prevention of mosquito infestations and on mosquito-related health risks and to inform citizens of the advances and new knowledge of scientific research in the field thus enhancing trust in science and research. Data and samples obtained thanks to the Citizen Science activities will be exploited by entomologists for increasing knowledge on mosquito species and distribution in Italy and for modelling human-mosquito contact.

Expected (or preliminary) results: A communication strategy integrating press releases, infographic materials and social media campaign (named #scattalazanzara) was designed and implemented to launch MosquitoAlert app (i.e. an application for mobile phone made available by the AIM-COST ACTION, www.aedescost.eu, by which citizen can send mosquito photos and record bites) both within Sapienza community and at the national level. Results of these activities implemented in the 2021 mosquito breeding season will be analysed in terms of engagement (e.g., citizens' response, interactions on the App and the numbers of downloads) and serve as the basis for 2022 and 2023 activities.

Future perspectives: The study aims to create the bases for appropriate dissemination and communication campaigns to be exploited in order to promote Citizen Science as a novel approach to provide data for increasing knowledge on mosquitoes to scientists, while raising awareness and promoting good preventive practices to contain mosquito nuisance and risk of mosquito-borne disease among citizen and to contribute to effectively shift from the “Public understanding of science model” to “Public engagement model”.

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