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VIII Seminar - PhD Day

Interdisciplinary approaches in Health Sciences: a bridge to the future

Istituto Superiore di Sanità
Rome, June 5, 2017

ABSTRACT BOOK

Edited by
A. Massimi, V. Pichler, I. Schietroma, G. Corano Scheri,
S. Paone, A. Martini, C. Kyriakou, R. La Russa,
A. Vullo and A. Mazzaccara

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Azzurra Massimi (a), Verena Pichler (a), Ivan Schietroma (a), Giuseppe Corano Scheri (a), Silvio Paone (b), Agnese Martini (a), Chrystalla Kyriakou (c), Raffaele La Russa (c), Annamaria Vullo (c) and Alfonso Mazzaccara (d)

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Bridges and creativity are the the two words will lead Phd - 8th Meeting - Infectious Diseases, Microbiology and Health Sciences. Bridging will be the mainstream concept, intended as connect and relate, to emphasize the multidisciplinary approaches as a method, to built up the future but also to send a message to those that believe in constructing walls. Creativity has been the main engine for science for centuries. Nowadays, the availability of advanced technologies, including omics approaches, give us the possibility to obtain a large amount of data in a reasonable time. In the last years, we have been more and more convinced that the problem was to get a good skill in the management of big data, just underestimating the role of our fantasy in the study design and of our capability of speculating possible scientific explanations. The Seminar, part of the collaboration between the Italian National Institute of Health, and the University of Rome La Sapienza, emphasizes the concept of the scientific method, coupling creativity and intuition with the most rigorous methodological approaches.

Key words: Research, Creativity, Microbiology, Infectious Diseases, Public Health, Social Medicine, Forensic Medicine

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Nell'ottava Giornata dei Dottorandi in Malattie infettive, microbiologia e sanità pubblica due sono le parole che indirizzano: ponti e creatività. Fare ponte, inteso come collegare e correlare, per sottolineare l'approccio multidisciplinare come metodo di lavoro per costruire il futuro ma anche per mandare un messaggio a chi preferisce oggi erigere muri. La creatività, invece, è stata il motore della ricerca per secoli. Oggi, la disponibilità di tecnologie avanzate, con particolare riferimento a quelle omiche, ci forniscono una grande quantità di dati in tempi relativamente brevi. Negli ultimi anni, abbiamo coltivato la convinzione che il problema fosse solo avere la capacità tecnica di analizzare tali dati, sottostimando il ruolo della fantasia nel formulare ipotesi e nell'analisi speculativa dei risultati. Il Seminario, nell'ambito della collaborazione tra Istituto Superiore di Sanità e l'Università di Roma la Sapienza, enfatizza il concetto di metodo scientifico, capace di coniugare la creatività e l'intuizione con gli approcci metodologici più rigorosi.

Parole chiave: Ricerca, Creatività, Microbiologia, Malattie Infettive, Sanità Pubblica, Medicina Sociale, Medicina Legale

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In loving memory of Anna Maria Patti

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Fiorenzo Conti

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Session 1

Health sciences, environmental chemistry, social medicine and forensic medicine

Chairpersons:

Arianna Giovannetti, Simone De Sio, Corrado De Vito

OCCUPATIONAL STRESS, ALCOHOL DEPENDENCE AND ALCOHOL CONSUMPTION

Stefania Fargnoli (a), Stefano Ferracuti (b)
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(b) Department of Neurology and Psychiatry, Sapienza University of Rome, Rome, Italy

At the beginning of the nineteenth century, Taylor, the founder of Taylorism, and his followers, including Ford, elaborated theories to adapt the "physical characteristics" of the human body to the machines ("*the right man to the right work*"), a formula that participated to the so-called "industrial miracle". Physical fatigue was considered as the only relevant variable and the worker was merely seen as a resource to be adapted to the machine for productive purposes.

Since that time, fortunately, significant progresses have been made. In the 60s "ergonomy" developed. The founder, Murrel, defined ergonomy as "the science that intends to adapt the work to the man". In the present form ergonomy poses particular attention to psychosocial risks in the workplace, in order to reduce job injuries and work diseases. The NIOSH (National Institute for Occupational Safety and Health) and the US Federal Agency operating in the prevention of work diseases, defines job stress as "the harmful physical and emotional responses that occur when the requirements of the job do not match the capabilities, resources, or needs of the worker ".

The European law enacted in these years, on one hand requires the employer to include in the risk assessment also the "work related stress", and on the other hand obliges the occupational physician to assess and evaluate alcohol consumption and dependence. The aim of this study is to assess the association between alcohol use and job stressors in healthcare workers. We administered questionnaires on seventy workers encompassing demographic data, alcohol use, occupational stress, depressive and anxiety symptoms.

The results seem to demonstrate a slight higher alcohol consumption in workers with higher occupational stress.

IDENTIFICATION AND QUANTIFICATION OF PSYCHOACTIVE DRUGS IN WHOLE BLOOD USING DRIED BLOOD SPOT (DBS) BY ULTRA-PERFORMANCE LIQUID CHROMATOGRAPHY TANDEM MASS SPECTROMETRY

Chrystalla Kyriakou (a), Silvia Graziano (b), Emilia Marchei (b), Roberta Pacifici (b), Enrico Marinelli (a)

(a) Unit of Forensic Toxicology (UoFT), Department of Anatomical, Histological, Forensic and Orthopedic Sciences, Sapienza University of Rome, Rome, Italy

(b) National Centre on Addiction and Doping, Istituto Superiore di Sanità, Rome, Italy

A procedure based on ultra-high-pressure liquid chromatography tandem mass spectrometry (UHPLC-MS/MS) has been developed and validated for the determination of twenty three psychoactive drugs from different classes, including cocaine, opiates, benzodiazepines, amphetamines, THC and some of their metabolites in whole blood using dried blood spot (DBS).

Simple and fast sample preparation was carried out before analysis. Briefly, pre-marked cards spotted with 30 μL blank blood, calibrators, QC and real samples were cut, once dried, at the edges and placed into a tube with 10 μL internal standards working solution (1 μg/ml) and 990 μL methyl alcohol. The tube was then sonicated for 15 min and centrifuged at 3,500g for 5 min. The supernatant was evaporated under gentle stream of nitrogen, re-dissolved with 100 μL UHPLC mobile phase (solvents A/B, 80/20, v/v) and 10 μL were injected into the chromatographic system.

Chromatographic separation was achieved at ambient temperature using a reverse-phase column and a gradient elution with two solvents: 0.1% formic acid in acetonitrile (Solvent A) and 5 mM ammonium formate at pH 3 (Solvent B). The separated analytes were detected with a triple quadrupole mass spectrometer operated in multiple reaction monitoring mode via positive electrospray ionization. The method was linear from the limit of quantification (5 ng/ml for all the analytes apart from 15 ng/ml for Δ-9-tetrahydrocannabinol and metabolites) to 500 ng/ml, and showed good correlation coefficients (r2=0.990) for all substances. Analytical recovery of substances under investigation was always higher than 75% and intra-assay and inter-assay precision and accuracy always better than 15%. Using the validated method, ten DBS samples, collected at the hospital emergency department in cases of acute drug intoxication, were found positive to one or more psychoactive drugs.

The major advantage of the here described method is the possibility to detect drugs even in 30 μL blood, with a simple sample collection and an easy pre-analytical treatment. Our data support the potential of DBS sampling for non-invasive monitoring of exposure/intoxication to psychoactive drugs. The current method could find application in both clinical and forensic toxicology analysis; in emergency rooms, roadside drug testing and workplace drug testing.

OCCUPATIONAL AND NON OCCUPATIONAL RISK FACTORS ASSOCIATED WITH SEROPOSITIVITY TO *ECHINOCOCCUS GRANULOSUS*

Agnese Martini (a), Serena Cavallero (a), Rita De Carli (b), Simona Gabrielli (a), Angelo Giacomi (a), Giovanni Luigi Milardi (a), Stefano D'Amelio (a)

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

(b) Sapienza University of Rome, Rome, Italy

Human Cystic Echinococcosis (CE), also known as hydatid disease, is an helminthic zoonosis caused by infection with the larval stages of the cestode parasites *Echinococcus granulosus*. CE continues to represent a global health hazard affecting approximately over 1 million individuals worldwide. Indeed, *Echinococcus granulosus* infection is globally distributed and found in every continent, except Antarctica. In endemic regions, human incidence rates for CE can reach greater than 50 per 100,000 person-years, and prevalence levels as high as 5-10% may occur in parts of Argentina, Perù, east Africa, central Asia, and China. *Echinococcus granulosus* may cause illness in intermediate hosts, generally herbivorous animals and people who are infected accidentally. Workers such as slaughters, tanners, stockbreeders, shepherds, butchers, veterinarians are at higher risk of the infection.

The present study aims to evaluate the seroprevalence of CE in workers exposed and in blood donors and to determine the prevalence of occupational and non-occupational risk factors associated with CE infection in both groups.

A cross-sectional study was conducted in a central region of Italy (Latium) in the period from September 2015 to September 2016. It included 177 workers exposed to biological risk of the *Echinococcus granulosus* infection (shepherds) and 192 apparently healthy blood donors selected from the same geographical area. General and medical information, including job history, occupational and non-occupational risk factors was collected using specific questionnaire. Human serum samples from shepherds and donors were collected and analyzed using a commercially available enzyme linked immunosorbent assay (ELISA) and seropositive samples were analysed further by Western blotting. Logistic regression was performed to evaluate the potential risk factors associated with the presence of antibodies. The results showed that 18 subjects (4.88%) were ELISA seropositive. High seropositivity was recorded in workers (5.65%), followed by the donors (4.17%). Only one seropositive sample was confirmed by Western blotting. The Individual Risk Score (IRS), based on sum of occupational and non-occupational risk factors, was associated to seropositivity (*P*=0.000 8; *OR*=1.889; 95% *CI*=1.689-2.113).

The results of this study reinforce the necessity to implement the prevention of risks at workplace, with special reference to the biological risk, using appropriate tools for the identification and the assessment of hazards combined with public health education and information.

VACCINE HESITANCY: KNOWLEDGE, ATTITUDES AND NEED FOR EDUCATION OF PREGNANT WOMEN REGARDING NEONATAL VACCINATIONS

Azzurra Massimi, Annalisa Rosso, Carolina Marzuillo, Corrado De Vito, Paolo Villari
Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

Vaccinations are one of the greatest achievements of Public Health. Nevertheless, they are not exempt from criticism and speculation that increase, especially in developed countries, the number of people who decide to delay or even to decline vaccinations, phenomenon also known as Vaccine Hesitancy. Our study aims to describe knowledge about vaccinations and intention to vaccinate of a population constituted by pregnant women.

Methods. A cross-sectional study was carried out (June 2016 - March 2017) through a questionnaire administered to 360 randomly selected pregnant women during their antenatal classes in 35 community Mother and Baby Centers in Rome (Italy).

Results. Mean age of respondents was 32.9 (±5.1) and 90% were giving birth for the first time. The most frequent source of information was by word of mouth (62.3%) or mass-media (45.0%). Only 35.8% of respondents received information on neonatal vaccinations from at least one healthcare worker, and the quality of the information provided was judged to be poor or insufficient by 21.3% of the respondents. Knowledge of vaccination schedule was insufficient since only 4% of the respondents knew exactly which vaccines were mandatory or recommended. Moreover, 23.5% of the women did not know that efficacy of vaccines is based on scientific evidence and the majority was uncertain (40.5%) or strongly convinced (14.1%) about the association between vaccines and autism, multiple sclerosis or cancers. A high level of hesitancy to vaccinate was found when women were asked for their intention to vaccinate their infants: 22.1%, 34.9%, 41.1% and 60.2% of respondents was uncertain about the use of hexavalent, MMR, MEN-C and Pneumococcal conjugate vaccines, respectively.

Conclusions. Lack of knowledge, uncertain reliability of the information source, limited attention from healthcare professionals and low quality of the information received appear to be the most relevant factors that may increase vaccine hesitancy. Pregnant women are a strategic target population for the development of communication and information plans, since pregnancy is a perfect time for learning (teachable moment). Health education programs are strongly needed, based primarily on the training of health workers as a vehicle of accurate information for the empowerment and development of a real "vaccine culture".

TELECARDIOLOGY: AN OPPORTUNITY FOR IMPROVE MEDICAL ASSISTANCE AND REDUCE HEALTHCARE COSTS

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Introduction. Saipem is a contractor company in Oil and Gas industry. Saipem has developed an in-house medical department, whose main objective, apart the management of medical emergencies, is prevention, health protection and promotion. In order to make these principals available and applicable at all site worldwide Saipem decided to initiate and develop the implementation of e-medicine in its daily operations. The aim of Saipem's e-medicine project is to provide assistance to physicians working in remote areas, where medical equipment is often the basic one and the local health care system is mostly rudimentary.

Methods. In 2007 an analysis of these needs came up with the idea and initiative, commissioning followed in practice with the services of "Telecardiology", to launch a project for telemedicine, which would find its application in the work, covering the three elements:

- support for emergency management;
- employee screening for the identification of specific cardiovascular risk and monitoring of those with known risks;
- health surveillance for cases where this and provided by legal regulations.

This would create a new type of telemedicine, in addition to those already known (remote consultation, home care, tele-education, etc.) The "care work" - medical care organization in the workplace. The site doctor had the opportunity to use the service in two modes: synchronous (real-time reporting) or deferred (reporting within 24 hours). The service, after the ECG was recorded, was activated by making a phone call to the number of dedicated Telecardiology Services Center.

Results. From the birth of telecardiology program (2007) we provided 19,325 ECG transmission. In 2016 we sent 3,448 cumulative ecg transmissions for specialist evaluation to Cardio Centre. 2,992 without any alteration in ECG. 456 showed major diagnostic criteria: Ischemic heart disease (14%), Arrhythmias (10%), Conduction defects (45%), increase in wall thickness or the size of the atra & veventricles (20%), other (11%).

Conclusion. Telecardiology rises in a cost-effective way the level health monitoring and cure of employees in remote locations. In 2016 the cost benefit analysis showed a saving of 865.440 Euros due to non-effected Medevacs.

USE AND UTILITY OF MICRO-RNA IN FORENSIC PATHOLOGY

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

The evaluation of vitality of a wound (whether it is produced *ante mortem* or *post mortem*) is crucial for the definite diagnosis of death. In particular, skin and bone lesions are often of peculiar importance. Immuno-histochemical techniques allow to evaluate the eventual presence of reactive processes occurring in the presence of vital lesions (several antibodies such as anti alpha- 1 chimotripsin, anti fibronectin, anti - TGF - alpha e TGF-beta 1, anti inflammatory cytokines, anti - TNF alpha, anti adhesion molecules, anti triptase, etc are available for this purpose). The analysis of bone samples can also provide useful information: for example, the detection of glycophorin - an integral transmembrane protein typical of erythrocytes - in bone samples is crucial for the diagnosis of death even after a long time.

Finally, microRNAs have recently emerged as candidate markers in forensic pathology. These small endogenous non-coding single stranded RNA molecules exert important regulatory functions and often present a tissue-specific expression. In particular, microRNA analysis is a challenging field of research in forensic science for the determination of skin lesions repairing processes and thus for the timing of these lesions. Our current research activity is addressed towards a panel of microRNAs which have been proposed as candidate targets with diagnostic power in forensic applications.

In conclusion, the analysis of skin and bone lesions in terms of vitality and timing is of crucial importance in forensic science in order to make a definite diagnosis.

HEALTH EQUITY: THE ROLE OF INTERSECTORAL ACTION IN REDUCING THE INEQUALITIES IN MIGRANT HEALT

Flavia Sesti, Maurizio Marceca
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The Bauman's liquid modernity highlights that the change is occurring more and more rapidly in the "modern" world, also due to the intensification of migrant flows.

In 2015 only, 244 million of migrants are counted in the world and 35 million of foreign residents in the European Union, more than 5 million of which in Italy. In this framework, new policies and actions are required, including in the public health sector. Under the light of Virchow's famous statement "Medicine is a social science, and politics nothing but medicine at a larger scale", social determinants assume a central value.

At international and national level, these new challenges are addressed in the European strategy "Europe 2020 - A strategy for smart, sustainable and inclusive growth" and in the United Nations 2030 Agenda for Sustainable Development.

Moreover, by adopting the recent "Strategy and action plan for refugee and migrant health in the WHO European Region", the World Health Organization (WHO) Regional Office for Europe confirmed the importance of a common approach: the current situation is seen an opportunity not only to deal with short-term needs but also to strengthen public health and health systems in the longer term.

At national level, in article 32 the Italian Constitution states health is a fundamental right of the individual and a collective interest, therefore free medical care is guaranteed to the indigent by the Republic. From this founding principle, the Italian National Health System provides health care to the migrants, yet the health policies have been suffering from challenges coming from other sectors, such as immigration.

A possible way forward is the Global Health approach, including the intersectoral action as described by the WHO. Through this, greater awareness of health, health equity consequences of policy decisions and organizational practice in different sectors can then be achieved, for a healthier public policy and practice across sectors.

As the Italian integration type causes a migrant insert in the low social-economic gradient and since everybody is affected by health inequalities, actions to improve the social determinants of health will result in a benefit for everybody.

Finally, the proportionate universalism approach proposed by Marmot (UCL-IHE) can permit to effectively tackle the social gradient with universal services responding to the level of need, recognizing more intensity of action to more disadvantaged groups for the same level of health.

Poster session

THE NEW APPLICATIONS OF THE SCIENTIFIC RESEARCH IN THE FIELD OF EVALUATION OF THE TIME OF DEATH: THE STUDY OF PMI THROUGH THE IDENTIFICATION OF NEW BIOMARKERS

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The time of death is one of the fundamental questions which the forensic pathologist is called to answer in the forensic work. Currently, the answer to this question comes from the study of chronology of death. It makes use of the analysis of abiotic and transformative processes. However, the diagnosis of the time of death is not accurate today because of the many variables that can make it uncertain. At present the field of forensic research for this purpose is involving molecular biology. In particular proteomics is a discipline that allows us the systematic identification of the proteome from the point of view of quantity and quality. Through the mass spectrometry it is possible to identify yet unknown molecules or to analyze that are already known.

The proposed operating model in this study is based on the application of proteomics and in particular the use of mass spectrometry, in the evaluation of the time of death of a corpse. The study involved the execution of peripheral blood samples of patients who died at the hospital departments participating in the research protocol with particular regard to the Intensive Care Unit. These samples were performed at predetermined time intervals, until 2 hours after death through the compilation of a data sheet reporting exact time of death (i.e., the zero time at which the first sampling has been carried out). Biological samples were analyzed later, after centrifugation, at the Department of Proteomics at the University of Catanzaro. Using an experimental approach, called "biomarkers discovery", any protein markers that have been identified and their quantitative or qualitative variations, during hours after death, could enable us to calculate the PMI (Post Mortem Interval).

The aims of the study are characterized by: evaluation of the expression changes of proteins in serum in different time intervals following the death; identification of protein candidates to become exclusive markers of time of death. These data will be used to create reproducible and repeatable operative models in the forensic field.

INTEGRATION OF MALDI-TOF MS METHOD IN HOSPITAL'S ANTIBIOTIC STEWARDSHIP PROGRAM: A MODEL OF CLINICAL-MICROBIOLOGICAL ALERT

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The main objective of this prospective study is to analyze the Matrix-Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS, bioMérieux, France) method in relation to antibiotic stewardship program with a type of structural intervention, oriented for microbiological specimen (blood cultures) and for setting (selected Hospital departments). In Intensive Care Unit, Emergency Medicine and Hematology Unit was activated a service of "clinical-microbiological alert" in collaboration with Infectious Disease Department of "Sapienza" University. All blood cultures consecutively tested positive with System BacT/ALERT® and confirmed microbial identification by MALDI-TOF MS method were first communicated to Infectious Disease Specialists (IDs). This alert started before confirmation of antibiogram susceptibility panel by VITEK®2 semi-automatic system. In the observation period (October 1, 2015 to March 31, 2017) have been collected data about 192 cases of clinical bacteremia identified as the same bacteria species isolated for single patient in a 30-day period. These represented 16, 5% of a total of 1,164 requested blood cultures in the selected wards. The source of the bacteremia was divided in 159 (83%) peripheral blood cultures and 33 (17%) central venous catheters blood cultures. A high rate of sentinel germs was detected, such as 67 (35%) Carbapenem Resistant *Enterobacteriaceae* (CRE), 10 (5,3%) Methicillin Resistant *Staphylococcus aureus* (MRSA) and 8 (4.2%). *Candida spp.* A gain of about 24 hour was observed in the identification of species with MALDI MS System compared to VITEK® alone. The IDs consultation was performed in 186 (96.8%) of cases within 48 hours.

We observed that the introduction of MALDI-TOF in a hospital lab definitely provides positive solutions in the choice of correct antibiotic treatment, especially in terms of rapid de-escalation. In this sense, MALDI-TOF is effective when integrated in the Antibiotic Stewardship Programs of the hospital. Further data analysis is requested to analyze impact on mortality of early initiation of antibiotic therapy and pharmaco-economis aspects of de-escalation after early species identification.

KNOWLEDGE AND PREVENTION OF CERVICAL CANCER AMONG FOREIGN WOMEN WITH AND WITHOUT A RESIDENCE PERMIT

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In the last decades, Italy has assisted to an increasing migratory flux.

It has been noted that immigrants - those with social vulnerability in particular - present major difficulties of access to sanitary services, including those of prevention; this happens due to lack of communication and information of available public services, as well as a lack of knowledge of all the opportunities of prevention.

Regarding the "Cervical cancer", most of the foreign women in Italy belong to the age group (25-64 years old), which is the target of mass screening offered free of charged by public health services. Upon the results of new studies it is shown that, for this people group, an increase in the likelihood of a late diagnosis of "neoplasia", obtained through a first level screening is observed.. The research will investigate the correlated variables and the effective access to the screening in the health facilities.

Through quantitative and qualitative methods, the research aims to examine their knowledge of screening (pap-test) and the effective adhesion to secondary prevention.

Finally, we attempt to investigate the appropriate strategies for this population "hard to reach", through collaboration of qualified voluntary health present in the city of Rome.

Data were collected through direct interviews of immigrant women on a weekly basis in an area particularly populated by immigrants, like Piazza Vittoria market. There the health service is provided by Caritas Diocesan of Rome in a project with ASL Roma1 which provides an information desk and directs people to the available public health services (including through the distribution of informational material prepared in several languages). The team is comprised of specialists from Caritas with the support of the youth in the civil service and volunteers.

Each month it is possible to access a specific program of cardiovascular and "cervical cancer" prevention, at the stand with the support of the ASL health personnel.

The study was conducted on 190 women. The majority of them had never made screening for lack of information (they never received an invitation from ASL, or did not understand the content in). Among women who have not carried out the screening an active information program was performed to ensure their protection.

A METHOD FOR SETTING THE EQUIPMENT AND FOR ESTIMATION OF MEASUREMENT UNCERTAINTY RELATED TO THE MICROBIOLOGICAL ASSESSMENT OF INDOOR AIR

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Indoor air contains a complex mixture of microorganisms, microorganism fragments, and byproducts such as endotoxins, mycotoxins, and volatile microbial organic compounds. Bacteria, fungi, viruses, protozoans, and microscopic animals have been linked to poor indoor air quality.

The air sampling in confined spaces can be monitored by active and passive methods; in active monitoring a microbiological air sampler physically draws a known volume of air through or over a particle collection device which can be a liquid or a solid culture media and the quantity of microorganisms present is measured in CFU (colony forming units)/m3 of air. Among the most commonly used active sampling systems there are single-stage samplers with orthogonal impact, such as the Surface Air System (SAS); such equipment ensure the removal of high volumes of air, but do not allow the direct intake flow control.

Air microbial sampling is a subject of great interest in different fields of human activity, however, generally accepted indications, concerning both the sampling methods to be used and the interpretation of the results, are still lacking; furthermore, it has been known that different active samplers show high variability giving different results in the same place at the same time. The use of a system, connected to the instrument and that consists of a Pitot tube and a manometer, has allowed (with the monitoring of environmental conditions and with fluid dynamic calculations) to determine indirectly the sampled air volume.

Evaluation of repeatability for both sampling and analytical phases and the subsequent statistical analysis of data, provided evidences for estimation of the associated uncertainty (carried out both the metrological and the Monte Carlo methods).

The implementation of the traditionally adopted official method for the determination of bioaerosols, will allow its use for the competence of testing and calibration laboratories (UNI CEI EN ISO / IEC 17025: 2005) in accordance with the general requirements.

THE STATE OF THE ART OF THE RELATION BETWEEN FEMALE'S BREAST CANCER AND THE EFFECTS PRODUCED IN THE COUPLE TWO YEARS AFTER DIAGNOSIS

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The World Health Organization (WHO) reports that, actually worldwide, breast cancer affects 18% of the female population; it's also estimated that 12.3% of women will be diagnosed with breast cancer in some moment of their lifes. Consequences of breast cancer can affect all the family and in particular the couple: psychosocial stressor not only has an impact on the quality of life of those who are suffering from the disease but also affects those who are close to the patient, in this case, the couple. Nowadays women have more survival posibilities and two years is considered a transition moment for restablishing relationships. In this study both quantitative and qualitative methods are used.

Objective. Effects produced in the couple after two years from the diagnosi of femal's breast cancer.

Methodology. An integrative review has been employed and inclusion and exclusion criteria have been defined. The period considered is 2000-2016 and the research has been performed through Mesh and non keywords analyzing Pubmed/Medline, CINHAL, Psycinfo and Web of Science's databas. Overall 1,936 articles have been found and after an evalutation process 21 of them have been retained.

Results. The results found in the literature that consider the last 5 years are the most important for articles production and knowledge development. The results can be summarized into three main categories: quality of life: there is a direct correlation between quality of life and age: to an advanced age diagnosis corresponds a greater quality of life with minor sequence and convercely; marital satisfaction: partners of women with breast cancer often go trough reactions that are similar to those of the patient. Spouses tend not to express their feelings and to shut themselves away (alexithymia) because they do not want to burden their partners with concerns that, according to the spouses, they can't bear; as a consequence spouses feel guilty for experiencing theese emotions and they feel powerless and deny their feelings; depression: it has been determined that economic and education variables are significative predictors for this category (to a greater economical stability and higher education corresponds minor depression and convercerly).

Conclusion. There is no doubt that the couple's dinamic is compromised when there is a breast cancer diagnosis in women. From the perspectivepoint of view, two years from the diagnosis, women seem to be ready to leave this experience behind themselves in order to reset their life. This transition generates a stress period known as "diadic stress" that includes the recovery process physical and emotional scars; the dyad has to adapt to this experience.The cancer becomes an experience of great suffering where some major questions, such as "what comes next?" are faced.

BACTERIAL FACTORS THAT PREDICT RELAPSE AFTER ANTI-TUBERCULOSIS THERAPY

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Background. We postulated that sub-breakpoint minimal inhibitory concentrations (MICs) of drug-susceptible *Mycobacterium tuberculosis* could predict relapse after tuberculosis (TB) treatment, and might serve as biomarkers for selecting treatment duration.

Methods. A retrospective case-control study of participants selected from Tuberculosis Trials Consortium Study 22 with relapsed and cured drug-susceptible TB. Pretreatment *M. tuberculosis* isolates were tested for sub-breakpoint isoniazid and rifampicin MICs, using custom microtiter plates and liquid culture tubes. We analyzed clinical, radiologic, and laboratory information. Mutation and RNAseq analyses were performed on a subset of isolates.

Findings. Fifty-five relapses and 63 cured controls were MIC-tested at increments below standard resistance breakpoints. Mean isoniazid and rifampicin MICs were significantly higher among relapses (P=0.003 and P=0.001, respectively). For rifampicin, the likelihood ratio of relapse increased with higher MICs, reaching 6.0 for MICs of 0.125 µg/mL. Isoniazid and rifampicin MICs were associated with relapse in a multivariable analysis (odds ratio, 2.75; P=0.002; and 1.37; P<0.005 for each 0.01 µg/mL increase in MIC, respectively) that included other significant patient characteristics (including ≥10% underweight, 8-week culture conversion, cavitary or bilateral disease on chest radiograph). Using both MICs, a receiver operating characteristic (ROC) curve analysis of relapse had an area under the curve (AUC) of 0.785, similar to an analysis that included all significant patient characteristics other than MIC (AUC, 0.776). The AUC of all significant patient characteristics (including MICs) was 0.888.

Interpretation. In drug-susceptible TB, sub-breakpoint MICs of pre-treatment *M. tuberculosis* isolates predicted relapse with overall performance comparable to all other patient characteristics combined.

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TRYPTOPHAN METABOLISM IN HIV-1 INFECTED PATIENTS: THE ROLE OF PROBIOTICS ON GUT-BRAIN AXIS

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Background. Alteration of tryptophan metabolism, which is caused by the activity of the interferon-inducible enzyme IDO-1, has an important impact on HIV-1 infected patients quality of life, in particular it could be involved in the onset of neurocognitive disorder. In fact, a number of study showed a correlation between an alteration in tryptophan metabolism, with production of neurotoxic metabolites, immune activation and neopterin production in the central nervous system. The dysbiosis and its related immune activation observed in HIV-1 infection are some of the main causes of IDO expression in the gastrointestinal tract. By modulating the gut flora with probiotics we hypothesized to impact on dysbiosis and on tryptophan metabolism, which doesn't seem to be appropriately controlled by cART.

Method. Ten HIV-infected subjects, under suppressive cART and undetectable viremia, underwent endoscopic procedures for the isolation of lamina propria lymphocytes (LPL), blood and feces collection and lumbar puncture for cerebrospinal fluid (CSF) collection prior to initiation of probiotics supplementation (T0) and after 6 months (T6). CSF neopterin levels were measured by ELISA assay. IDO mRNA levels were measured by real-time PCR in both PBMC and LPL. Tryptophan level were quantified in the fecal samples through 1H-NMR analysis, and plasma serotonin levels were measured by ELISA assay. All measurements were performed at T0 and T6. Data were analyzed by Wilcoxon test.

Results. We found that plasma neopterin were significantly lower at T6 compared with T0. Moreover, a significant reduction in IDO mRNA expression in both LPL and PBMC at T6 is observed. Finally, related to tryptophan metabolism, we observed a significant reduction of tryptophan in the feces and an increase in the levels of plasma serotonin, which is a direct product of tryptophan metabolism.

Conclusions. We highlighted a relationship between probiotic supplementation, inflammation and serotonin levels. Overall our preliminary results indicate that probiotic supplementation could reduce neopterin levels in CSF, modulate tryptophan metabolism, through the reduction of IDO expression, and increase the levels of plasma serotonin, in order to reduce the side effects of the deregulation of tryptophan metabolism and its catabolites on the neurocognitive disorders of HIV-1 population.

GAMBLING AMONG TEENS IN ROME

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Gambling Disorder (GD) is considered as a behavioral addiction or dependence "sine substantia". In 2013 DSM-V classifies GD in the dependency section (Substance-Related and Addictive Disorders) for its similarities between this and addictions to alcohol and other addictive substances. The European School Survey Project on Alcohol and other Drugs (ESPAD) conducted a survey that sets itself the objective to monitor the consumption of psychoactive substances, legal and illegal, and other risk behaviors in the Italian school system. Throughout 2014, ESPAD conducted a survey on GD among 15-19 year-old school students: amongst the 86.1% of non-gamblers, 6.0% represent social gamers, 4.2% of those with issues and 3.7% of those pathological problems. In the last years Italy implemented World Health Organization indications on compulsive gambling as being a clearly identified morbid form and that in the absence of appropriate measures of information and prevention, it can represent, as a cause of its spread, an authentic social disorder. In this regard with the Balduzzi Act (November 8, 2012, n.189 art.5), gambling addiction has been included in the Italian National health service (LEA).

The project addresses the need for:

- quantifying the prevalence of the phenomenon in a middle school students population in order to identify those at risk/affected by GD;
- analyze items through specific behaviors typical of gamblers possibly associated to the loss of control and risk behaviors;
- determine the level of perception of the health risk associated uncontrolled use of games in the population of students in the city of Rome.

An observational study was conducted in high schools in the city of Rome. The sample consisted of 282 students (130 males and 144 females) aged from 15-19 years. The project involved 2 schools in the center and two schools in suburbs. Three anonymous questionnaires were administered: 1) The South Oaks Gambling Screen Revised For Adolescents (SOGS-RA); 2) Short Form Health Survey36 (SF-36), which assesses the state of health in general, Risk Taking Behavior Questionnaire- For School (RTBQ-FR)

So far the analyzed test is the SOGS-RA which has previously shown that 3% of the students are pathological gamblers, 4.5% only problematic gamblers; among these two students have declared they said they had asked for money to usurers. The sample results showed that 22 students out of 282 plays to escape problems or to relieve feelings of dysphoria; 19% of students did not answer this question.

ASSESSMENT OF THE ACTIVITY OF N-ACETYLCYSTEINE AGAINST CARBAPENEM RESISTANT ACINETOBACTER BAUMANNII

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Introduction. There are few treatment options to control infections caused by multi-drug resistant (MDR) *Acinetobacter baumannii*. Our aim is to identify molecules not antibiotic that can interact with the different bacterial metabolic pathways and to establish a synergy with specific antibiotics.

Materials and methods. We started to focus our attention on 10 strains of *Acinetobacter baumannii* resistant to Carbapenems (CR-Ab). The phenotypic characterization of bacterial strains was evaluated by the Hodge modified test and sensitivity/resistance to temocillin. We evaluated the MIC for N-Acetylcysteine (NAC), Ampicillin Sulbactam (A/S), Meropenem (MER), Rifampicin (RIF), Colistin (COL) and Tigecycline (TIG) with macrodilution broth. The checkboard method with calculation of FIC-index was performed to determine the synergy between different combinations of NAC and antibiotics, both at sub-inhibitory concentrations. Furthermore, we performed time kill curves of beta-lactams + NAC combinations.

Results. Of the 10 strains analyzed, the phenotypic results were concordant with the presence of OXA carbapenemase. The MICs50/90 were 128/512 µg/ml for MER, 64/256 µg/ml for A/S, 2/4 µg/ml for RIF, 0.25/4 µg/ml for COL, 0.5/1 µg/ml for TIG respectively. The MICs 50/90 for NAC were 2.5/5 mg / ml. The synergism between NAC and antibiotics showed a FIC - index<0.5 in 90% (MER+NAC), <0.5 in 90% (A/S+NAC), <0.5 in 80% (RIF+NAC), >0.5 in 70% (COL+NAC), >0.5 in 100% (TIG+NAC). The TKC gave the following results: at a concentration of 2.5 mg/ml (sub-inhibitory concentration) NAC reached full bactericidal activity in the first 2h. Sub inhibitory concentrations of NAC, together with concentrations obtainable in the serum of MER and A/S are watched within 24 h showing complete synergy between NAC and the 2 β - lactams.

Conclusions. We showed that NAC in combination with other antibiotics commonly used in therapy to fight CR-Ab infections (Carbapenemase-Resistant-Antibiotics such as meropenem), exhibits high synergistic and bactericidal activity. These results are probably due to the strong nucleophilicity possessed by NAC which is able to create a strong internal entropy in the bacterial cell by the breaking of disulfide bonds. The role of NAC together with other antimicrobials deserves further investigations.

URINARY LEVELS OF AFLATOXINS IN PROFESSIONALLY EXPOSED WORKERS

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The preliminary data for this PhD project are presented. The data derives from the analyses performed by ISS in the framework of a lately concluded research project coordinated by the AUSL Reggio Emilia and supported by Emilia Romagna region.

Feed mill workers may handle or process maize contaminated with aflatoxins (AFs). This condition may lead to an unacceptable intake of toxins deriving from occupational exposure. To assess the serological and urinary levels of AFs in workers exposed to potentially contaminated dusts in two Italian mills, blood and urine samples were collected (from March to April 2014), on Monday and Friday morning of the same working week from 29 exposed workers and 30 non-exposed controls. AFs (B1, B2, G1, G2 and M1) and aflatoxicol (AFOH) were analyzed. Moreover, each subject filled in a questionnaire to evaluate potential food-borne exposures to mycotoxins; in addition, also AFs contamination in environmental dust was measured in both plants.

No serum sample was found to be positive. Seventy four percent of urine samples revealed AFM1 presence. AFM1 mean concentration was 0.035 and 0.027 ng/ml in exposed and non-exposed workers, respectively (p=0.432); the concentration was slightly higher in Friday's than in Monday's samples, in exposed workers, 0.040 versus 0.031 ng/ml and non-exposed controls (0.030 versus 0.024 ng/ml; p=0.437). Environmental AFs contamination ranged from 7.2 to 125.4 μg/kg. The findings of this study reveal the presence of higher AFs concentration in exposed workers than in non-exposed controls, although these differences are to be considered consistent with random fluctuations.

The presence of the mycotoxin itself, namely AFB1, in urine and serum, is reported to represent only the 0.2% of the total toxin intake; while AFM1, which is one of the AFB1 metabolite, represent about the 1.2÷2.2%. In order to confirm the different AFs concentrations between exposed workers and controls, the analysis of other, more abundant, AFs metabolites may represent the best strategy to define AFs exposure deriving from both, food consumption and environmental contamination. However the absence of commercially available standard for such metabolites requires an upgraded instrumentation. Therefore, the follow up of the presented study will be the analysis of AFs metabolites with high resolution mass spectrometry of the same urine and serum samples in order to overcome the analytical problems and to better support the differences in AFs levels between exposed workers and controls already highlighted in the preliminary data presented.

PLASMODIUM VIVAX AND FEVER OF UNKNOWN ORIGIN IN THE WEST REGION, CAMEROON

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Plasmodium vivax (P. vivax) is considered as absent in West/Central Africa because of the high prevalence of Duffy antigen negativity in the local human population. Duffy antigen on red blood cells is the only well-known receptor allowing the entry of *P.vivax.* However, in recent years, several studies reported P. vivax infections in sub-Saharan Africa among Duffy negative individuals as well as arboviruses circulation. Our research aims to assess the possible circulation of *P. vivax,* other *Plasmodium spp,* arboviruses *(Dengue, Chikungunya, Zika* viruses*)* and molecular factors linked to the susceptibility to *P. vivax* and the pharmacogenetics of its treatment (Duffy antigen, G6PD deficiency, CYP450 genetic variability) among outpatients reporting fever and attending health facilities in Santchou and Dschang Health Districts (West-Cameroon), located at 700 and 1,400 meters above the sea level respectively. Samples collection was performed using dried blood spots during the dry season (December-February) in Dschang and rainy season in Santchou (August-December). All samples were analyzed by molecular conventional methods (PCR).

In total, 884 samples were collected and malaria parasite DNA was detected in 247 (27.9%) samples. In particular, 241 cases of *Plasmodium* mono-infections (212 *P. falciparum*, 26 *P. vivax*, 2 *P. ovale*, 1 *P. malariae*) and 6 cases of co-infections (3 *falciparum/vivax*, 2 *faciparum/ovale*, 1 *falciparum/malariae)* were detected. Globally, *P. vivax* has been detected in 29 cases (11.7% of positive samples), mainly from Dschang (n=27) than Santchou (n=2). All the *P. vivax* positive cases have shown a Duffy-negative genotype (-33CC). Further analyses are still to be done concerning human genetic and arboviruses detection. Our data show, for the first time to our knowledge, the circulation of *P.vivax* in the West Region of Cameroon among Duffy-negative autochthonous individuals, with a prevalence possibly depending from altitude and seasonality. Further data are necessary in order to assess the real *P. vivax* local circulation, as well as to

identify Duffy-independent *P. vivax* erythrocyte invasion pathway. Furthermore, in a public health point of view, it is necessary to improve the local microscopic diagnostic capacity in order to ensure a more effective and safer therapeutic management of vivax malaria attacks and relapses.

INFECTIONS RELATED TO THE HEALTH CARE IN DEPARTMENTS OF INTENSIVE CARE. STUDY IN A RTI

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Every year in Europe 4,100,000 patients get infections related to health care (ICA) and about 37,000 of them *die* because of it, furthermore indirectly 110,000 *die* for infections linked to ICA.

Esteemed costs of ICA are around 6,000,000,000 €. The most frequents ICA are about urogenital and respiratory apparatus, septicaemias and post-surgical infections.

20-30% of ICA is prevented through good hygiene practices. The highest percentage of dead linked to ICA is due to hospitalizations in Departments of Intensive Care (RTI). For this reason our research is finalized to identify environmental standards linked to finding microorganisms guilty of ICA and cases of ICA in RTI.

We observed Neurosurgical RTI in a huge roman hospital over a term of around 18 months (October 2015 - March 2017), monitoring indoor microbiological air quality and some critical surfaces: bedside, pharmaceutical cart and monitor; and some physical microclimatic standards which are air temperature (Ta), relative humidity (HR) and air speedy (Sa), with a related evaluation of heat wellness which certainly influences workers' behaviour and the development of helpful practices both nursing and medical.

The partial data collection related to critical surfaces stress some non-compliances, in some samples we isolated environmental pathogenic microorganisms: *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Pseudomanas aeruginosa* e *Staphilococcus aureus* methicillin-resistant.

Regarding the total microbial mesophilic count at 37°C, it results non- compliant compared to the limit of 50 ufc/24 cm2 in 17,77% bedside samples, in 4,34% of samples pharmaceutical cart and 1,96% of monitor samples. Microbial density resulted variable from a minimum level of <1 ufc/24cm2 found on pharmaceutical cart to maximum level of >300 ufc/24 cm2 found on bedside.

In the remaining months of research with the definitive elaboration of the available results, we try to relate the physical standards above-written with microorganisms found on inanimate surfaces bordering client's bed, to understand in which way and how much they could contribute to their survival.

The results stress the need to maintain a high attention on protocol sanitation application of critical surfaces and operating guidelines linked to healthcare, to guarantee a high hygienic standard.

PLASMA RIBAVIRIN CONCENTRATION IN HCV CIRRHOTIC PATIENTS TREATED WITH DIRECT ACTING ANTIVIRALS (DAAS)

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Ribavirin (RBV) may still be necessary in treating HCV cirrhosis with Direct Acting Antivirals (DAAs) in spite of dose-limiting hemolytic anemia. Plasma RBV levels are reported to drive the intracellular phosphorylation rate of RBV; however plasma RBV kinetics during DAA treatment have not been fully elucidated.

The aim of the study was to examine RBV and Hemoglobin (Hb) kinetics in cirrhotic patients during DAA treatment.

43 HCV consecutive cirrhotic patients treated with DAAs and weight-based RBV for 12 or 24 weeks have been enrolled. 79% were HCV genotype 1 infected patients, 28% were naïve, 21% were diabetics, 23.3% had hypertension and 28% had esophageal varices. Patients were treated with different interferon free regimens, 88% of which containing sofosbuvir. Plasma samples were collected at week 1, 2, 3, 4, 6, 8, 10 and 12 to evaluate RBV and Hb plasma levels (RBV-L, Hb-L). RBV dose was modified in patients with anemia, defined as Hb loss of ≥2 g/dL as compared to baseline and/or Hb levels ≤10 g/dL. RBV-L at week 4 were compared with values of 20 PEG-IFN and RBV treated controls.

Sustained virologic response (SVR-12) was 95%. Median RBV-L at week 4 were significantly higher in DAA compared to PEG-IFN/RBV treated patients (3.8±3.1 *vs* 1.9±0.9 mcg/ml; p=0.014) and a significant interpatient variability in the dose/RBV-L ratio was observed. RBV dose was reduced in 25 pts (58%), 21 (84%) within 4 weeks of treatment, RBV-L remained above 2 mcg/ml in all and SVR was not affected. RBV dose reduction was associated with age, gender, GFR and RBV-L at week 1 ($p<0.05$). After controlling for the effect of e-GFR and RBV dose, RBV-L was on average higher in females, increased up to 6 weeks and declined thereafter.

A sharp, early rise of RBV-L with great inter-patient, gender-associated variability was observed in HCV cirrhotic patients treated with DAAs. Early (week 4) RBV dose reduction was often needed due to anemia, but did not affect SVR. After controlling for the effect of gender, e-GFR and RBV dose, RBV-L tended to spontaneously decrease after 6 weeks of treatment indicating a possible metabolic adaptation. Hb kinetic may safely guide individual adjustment of RBV dose.

MALPRACTICE CLAIMS: A RESOURCE FOR THE IMPROVEMENT OF CLINICAL RISK MANAGEMENT

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In recent years, there has been a meaningful change in the relationship between the doctor and the patient due to an increase in the social perception of the medical malpractice issue. This phenomenon has led to an impressive increase in civil litigation relating to medical professional liability with evident consequences on the costs for Health Care Systems and, above all, on issues concerning risk management and patient safety.

The threat of litigation generates a reluctance among physicians to report sentinel events, errors, and negligence with resulting in the inability to improve pro-active clinical risk policies and reduce the phenomenon of defensive medicine.

The analysis of data arising malpractice claims suggests interesting insights that can increase our understanding of suboptimal health care and encourage the development of planning tools for health care. This project was conducted at the Umberto I General Hospital in Rome, a health care facility which can count 1,326 beds including 1,184 for hospitalization and 142 for Day Hospital admission. The database includes 1,391 malpractice claims recorded from 2007 to 2017, managed through a self-insurance plan.

This preliminary investigation aims to evaluate the potential role of litigation data in reducing medical error and physicians' risk of liability, improving patient safety, and decreasing costs for Health Care Systems through the analysis of variation among specialties, diagnostic and therapeutic procedures involved, complications and type of harm alleged. The results obtained can be used to support pilot studies to improve and implement the standard clinical practice, guidelines, and protocols to be used within the hospital. The added value of this study consists of the proposal of a methodological approach to the litigation cases aimed at improving the performance of health facilities with attractive implications in relation to the provisions on risk management policies contained in the recent reform of the professional liability of the healthcare professions operators (artt. 1-4 Law no. 24/2017).

In conclusion, the relevance of the data collected shows interesting perspectives in terms of clinical risk management to improve healthcare quality and sustainability of the health system.

PERFLUORINATED COMPOUNDS IN HUMAN SERUM: METHOD SETTING-UP FOR BIOMONITORING

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Background. Perfluorinated Compounds (PFCs), such as perfluorooctane sulfonate (PFOS) and Perfluorooctanoic Acid (PFOA), have been produced since the 1950s and are used in many industrial and manufacturing applications, including production of nonstick cookware, waterproof and breathable textiles, and protective coatings for paper, food packing materials, and carpets. PFCs comprise a heterogeneous class of chemicals consisting of an alkyl chain (4-14 carbons), which is partially or fully fluorinated, and have different functional groups attached. PFCs are commonly detected in wildlife and human blood samples. Blood samples of occupationally exposed individuals and the general human population in various countries were found to contain PFOS and PFOA at measurable levels. Children often showing higher serum concentrations than adults. Food intake appears to be the major factor contributing to background PFC levels in human sera.

Methods. Has been developed an on-line Solid-Phase Extraction (SPE) method coupled to High-Performance Liquid Chromatography (HPLC)-tandem Mass Spectrometry (MS/MS) for measuring trace levels of Perfluorooctane Sulfonamide (PFOSA), 2-(N-ethyl-perfluorooctane sulfonamido) acetic acid (Et-PFOSA-AcOH), 2-(N-methyl-perfluorooctane sulfonamido) acetic acid (Me-PFOSA-AcOH), perfluorohexane sulfonic acid (PFHxS), PFOS, PFOA, perfluoroheptanoic acid (PFHpA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDeA), perfluoroundecanoic acid (PFUA), and perfluorododecanoic acid (PFDoA) in serum. Without protein precipitation, only dilution with 0.1 M formic acid, one aliquot of 100 µL of serum was injected into a commercial column switching system that allowed for concurrent SPE and HPLC-MS/MS acquisition. First, the analytes were concentrated on a C18 SPE column. Then, this column was placed automatically in front of a C8 analytic HPLC column for chromatographic separation of the analytes. Detection and quantification were done using negative-ion TurboIonSpray ionization, a variant of electrospray ionization, MS/MS.

Results and conclusions. The calibration curves showed adequate linearity (correlation coefficients 0.97-0.99). The method accuracy was assessed by five replicate analyses of serum spiked at three different concentrations and expressed as a percentage of the expected value. Above the LOD, the intraday variability, reflected in the standard accuracies (83-104%) and their relative standard deviations (5-16%).

Recovery ranged between 85-110% for all analytes. The high throughput and low limits of detection (0.03-0.4 ng/mL) using a small sample volume (100 μL of serum) and isotope dilution quantification make this method suitable. Method is appropriate for the simultaneous quantitative determination of PFCs for large epidemiologic studies to assess the prevalence of environmental exposure to PFCs.

ASSESSMENT OF MARKERS OF ANTIMALARIAL DRUG RESISTANCE IN *PLASMODIUM FALCIPARUM* ISOLATES FROM TWO AFRICAN ENDEMIC COUNTRIES

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Artemisinin-based Combination Therapy (ACT) is the most effective anti-malarial treatment for *Plasmodium falciparum* malaria. The introduction of ACT as first-line drug has led to extraordinary results in the control of the disease, especially in sub-Saharan Africa. However, the emergence and spread of resistance to artemisinin in the Southeast Asia jeopardizes these results. Moreover the extent of artemisinin resistance in Africa should have to be considered as an epochal disaster. The very recent identification of the molecular marker for artemisinin resistance in *P. falciparum*, the K13 propeller gene, give us an important tool for monitoring the possible spread of *P. falciparum* isolates resistant to artemisinin derivatives.

In this scenario, we screened 127 *P. falciparum* isolates from Chobe, Okavango and Ngami districts in Botswana and 43 isolates from Guinea Conakry to investigate the presence of polymorphisms in the K13 gene, by PCR and direct sequencing. In Botswana the first-line ACT for treatment is Artemether-Lumefantrine (AL), while in Guinea Conakry, the first-line is Artesunate-Amodiaquine (AS-AQ) or AL.

In the present work, we identified the two known synonymous mutations, R513R and V555V, in three *falciparum* isolates from Botswana. Non-synonymous mutations were not identified in this country. Two non-synonymous mutations, G538S and A578S, were detected in two isolates from Guinea Conakry.

Additionally, polymorphisms in *pfmdr1* gene were also analyzed to monitor the possible emergence of the amodiaquine and lumefantrine resistance.

This preliminary results showing the detection of polymorphism in the K13 gene suggests the need of further investigation in these study areas.

FRONTAL SINUSES FOR IDENTIFICATION: VALIDATION OF THE SEMI-QUANTITATIVE CAMERIERE'S METHOD

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Comparison of *ante mortem* and *post mortem* records is an important procedure in identifying individuals. Many parts of the skeleton can be used for this purpose: teeth, shoulder, skull, sphenoid sinus, sella turcica and frontal sinuses.

In 1987, Yoshino et al. proposed a system of classification of the frontal sinuses based on the following morphological characteristics: area size, bilateral asymmetry, superiority of area size, outline of superior borders, partial septa, and supraorbital cells.

This system assigns a class number to each morphological characteristic and the frontal sinus patterns of a given person are formulated as a code number obtained by arranging the class numbers in each classification item as serial numbers. In the present study, the importance of Yoshino's identification system is confirmed, possible errors in comparisons between *ante mortem* and *post mortem* X-rays are examined, and potential corrections are proposed. We considered a system of classification of the frontal sinuses based on the following morphological characteristics: SOR1 and SOR2, instead of the area size and bilateral asymmetry of the Yoshino's method, and superiority of area size, outline of superior borders, partial septa, and supraorbital cells. The frontal sinus pattern was classified according to the bivariate continuous variable SOR=(SOR1, SOR2) and the five discrete variables: Ss, Ou1, Ou2, PsandSc. We assumed that SOR was a bivariate normal random variable. We had to take into account two possible errors: α) two X-ray images of the same skull in different positions are not recognized as belonging to the same individual (false negative identification); β) two X-ray images of different skulls are identified as belonging to the same individual (false positive identification). False negative identification, α, is mainly due to the different skull position with respect to the X-ray beam. Since measurements concerning the frontal sinus area revealed high intra-individual variability, we replaced this morphological item by SOR, which showed a lower intra-individual coefficient of variance in different skull positions.

The probability of false positive identification, β, was evaluated using a bivariate normal distribution, and its unknown parameters (expected values, variances, correlation coefficients) were estimated from sample data. The estimate of probability β in our example was obtained using a PC computer program written in S-language. The present research, carried out on 90 x-ray imaging provided by the Department of Radiology of Sapienza, University of Rome, reveals the usefulness of frontal sinus patterns in the field of personal identification, also taking into account that our adjustments significantly decreased probability of misidentification of unknown skeletal remains.

DRIVING UNDER THE INFLUENCE OF DRUGS: ANALYSIS OF DRUGS AND MEDICINES IN ORAL FLUID

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In 2010, the Italian "street code" was modified regarding the regulation of "driving under the influence of drugs" but yet in 2017, the underlying problem of drug-driving has not been solved due to many reasons and a straightforward procedure for Police Forces to contrast this phenomenon does not yet exist. This research project aims at evaluating those issues related to different aspects (legal, scientific, economic, burocracy…) and finally defining an operative protocol, including a validated analytical method in order to find drugs or medicines in oral fluid (OF).

The project methodology foresees:

- study of the current Italian law framework which highlights some issues and gaps;
- study of biological fluids, the definition and testing of a "on the street oral fluid collection" procedure;
- performance assessment of tools currently available on the market which allow a quick analysis of drugs presence in oral fluid;
- development and validation of a chemical-analytic method for qualitative-quantitative analysis of drugs in oral fluid based on UHPLC-MS-Orbitrap (Ultra High Pressure Liquid Chromatography).

Art. 387 of the Italian "street code" has two major critical aspects that undermine Police Forces works in terms of both interpretation and actual application of the law itself:

- it does not have the so called "zero tolerance" principle like in other European legislations and yet "no minimum quantity presence" for each substance has been defined leaving a grey area and a great degree of interpretation;
- the regulation aiming at defining recognition methodologies and related tool has not yet been released.

The assessment of biological fluids characteristics has confirmed saliva to be the ideal choice for conducting analysis related to the use of drugs, in those kind of cases, due to the following advantages related to saliva collection that:

- is considered not-invasive from a legal standpoint;
- is less risky for the officer in charge and it does not require specific skills;
- is less expensive and faster.

A preliminary assessment of the whole procedure was performed by using 100 screening-tests on actual cases collected on the streets of Rome. These samples helped fine-tuning the procedure and supported the performance test of the tools and analytic method.

SCREENING FOR CELIAC DISEASE AMONG THE PERSONNEL IN SERVICE IN AN ITALIAN ARMED FORCE

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Background. Celiac Disease (CD) is an inflammatory life-long enteropathy, whose prevalence in Italy is roughly 1%. CD shows up with signs and symptoms ranging from mild to very severe. In the latest years, a growing number of asymptomatic patients have been diagnosed with CD in the course of screening programs among general population or CD first-degree relatives.

Aim of the study. To study the CD prevalence among the personnel of an Italian armed force. This population has been identified as target of a CD screening because the militaries undergo a check-up at the enrolment to state their physical ability to serve and they carry out a physical demanding job.

Material and Methods. The study is approved by the ISS Ethical Committee (568/16). All the personnel admitted to the Health Service of an Italian Armed Force since February, 01 2017 is asked to participate. Their plasma is tested anti-tG IgA levels by an ELISA kit (Eurospital, Trieste, Italy; cut-off 9 UI/ml). Positive individuals are investigated for EMA and eventually, duodenal biopsy. A questionnaire with the relevant clinical information is filled out by the enrolled individuals.

Preliminary Results. Eighty-two militaries (74 M, 8 F age range: 18.2-66.5 ys) were enrolled. One (M; 66.5 ys) was positive for anti-Tg (40 UI/ml) and then checked for EMA, resulted negative. This patient has chronic kidney failure and pancreatitis, so the CD autoimmunity might be related to these concomitant conditions. A military had a previous diagnosis of CD and is on a GFD; his anti-tG levels were <9 UI/ml, indicating a good compliance to GFD. Questionnaire have not yet been analyzed.

Conclusion. The CD prevalence among military personnel, so far, is 1/84, similar to that of the general population.

THE IMPACT OF CHRONIC NON-CANCER PAIN THERAPY ON THE QUALITY OF LIFE OF PATIENTS. A MULTI-CENTRE SURVEY OF PAIN MANAGEMENT CENTRE NETWORKS IN ROME

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Introduction. Data from international literature highlight the negative impact of chronic non-cancer therapy pain on Quality of Life (QoL) of cancer patients. The QoL is a multidimensional concept determined by objective and subjective factors. However, the data improve after patients undergo four, six week, or/and six month multidisciplinary treatment regimens. Pain Management Centers (PMC) were established in Italy in 2010 to guarantee patients with acute and chronic pain effective and appropriate treatment. So far, there have not been studies in Italy evaluating the impact on the QoL of patients treated in PMC.

Objective. The study aims to monitor the effects of treatment provided in PMC on subjective and objective aspects of the QoL of patients with chronic non-cancer pain.

Materials and Methods. A multicenter qualitative-quantitative prospective study of the population regarding PMC in Rome. The survey was carried out at the treatment centers of the ASL Rm2, Cristo Re Hospital and at the Hospital of San Giovanni Addolorata di Roma. The instruments chosen to conduct this survey include Euroquol 5D - Neck Disability Index or Oswestry Disability Index 2.1a -Brief Pain Inventory - Hospital Anxiety and Depression Scale-Pittsburgh sleep quality index. The evaluation and monitoring of the results was performed at time zero, 1 month, 3 months, 6 months, as recommended by the International Association for the Study of Pain.

Results. 300 patients were enrolled in the study and 1200 surveys were conducted. The data gathered showed that the pain experienced by patients, according to its intensity, has significant repercussions on quality of life limiting physical and psychological functions as a result heavily affecting the patients' joy of life.

Conclusions. Treatments carried out at PMC require comprehensive, multidisciplinary and interdisciplinary approaches, which involve pharmacological treatments and complementary and invasive interventions that match individual patients health care needs. Each subject suffering from pain must be treated singly, where psychological, emotional and cognitive characteristics are integral parts of one's perception of the same pain. Today, there seems to be inadequate adherence of PMC multidisciplinary regimes, both in terms of evaluation, and multidimensional treatment of chronic benign pain.

EVIDENCES FROM THE PROJECT "HEALTH SURVEILLANCE FOR THE VOLUNTEERS IN THE THIRD APPLYING ART. 3 OF THE ITALIAN DL 81/2008"

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Introduction. Significant data about the health conditions of volunteers of the third sector where found after 3 years from the beginning of the PhD project.

Description. the team kept performing the medical examinations according to the protocols identified and experimented them in different territorial areas to verify their applicability according to the territory in which volunteers operate. Between Val D'Aosta, Teramo, Rome and province approximately 1500 subjects were visited. The team finished the standardization of the specific risks to which volunteers are exposed considering their everyday tasks and licenses they have and referring to the inherent risks of the civil protection activities defended already by the current legislation. Final changes to the forms used were made to avoid redundancy and to simplify the health records. The population of the examined volunteers was composed by: about 25% of subjects older than 60 years, 6% of subjects between 59 and 50 years old, 30% between 49 and 40 years old, 20% between 39 and 30 years old, 18% between 29 and 20 years old and 1% younger than 20 years old.

Evidences. The analysis of the data obtained outlined that only 25% of the population examined, exposed on duty to blood borne pathogens, had received HBV vaccination. Of this 25%, 10% were health-care workers who were vaccinated already at their workplace and 15% were people who were born after 1978 and covered by the mandatory vaccination campaign performed on general population by the National Health System. With the introduction of our Health Surveillance protocol, it was necessary to take an urgent vaccination campaign to give the necessary protection to the whole population in voluntary service examined and make sure that the subjects previously vaccinated still had a protective HBsAb title. To define the frequency of the health surveillance examinations, finding out a very slight distinction between the volunteers exposed to the general risks and those who may need further investigations, we proceeded taking into consideration the age of the subjects and the amount of hours in voluntary service as described in the legislation: less than 250 hours, between 250 and 535 and more than 535 annual hours of volunteer service.

Conclusions. With our protocol we aim to ensure plain safety to all the volunteers working in the third sector.

BIOLOGIC AND BIOSIMILARS, LEGAL AND FORENSICS ISSUES

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The expiration of patents of the first biologic, after 30 years, created the opportunity to develop drugs so called Biosimilars, or similar drugs to a reference biologic product already authorized in the EU and for which the copyright has expired.

The possibility of the introduction of such drugs, and its expense reduction for the National Health Service (at least 20%), it gave fount to a broad and thorough debate on their usefulness and their automatic substitution to the originator. The marketing of biosimilars, and biologic ones, in Europe is authorized by the European Medicines Agency (EMA), but the evaluation of automatic substitution is left to the individual national Authority, in Italy AIFA. The latter has published a first position paper in which substantially excluded automatic substitutability, since the "reference biological medicinal products and biosimilar medicines are similar, but not identical"; now it prepares to publish a second position paper, which, at present, has such founding and innovators points compared to the first one: a) does not make mention of naive patients, while previously infer that the biosimilars were basically meant for such patients; b) it overlaps the therapeutic efficacy and safety that had once biosimilar recognized by the EMA, extending also this principle to the extrapolating the of therapeutic indications, its EMA that establishes whether the therapeutic indications originator can be transferred to its biosimilar; c) it leaves in any case, the decision on the introduction or moving between a biological and a biosimilar, the prescribing physician, considering, however, the biosimilar therapeutic option for which the risk-benefit ratio is the same as that originator of the corresponding reference.

In anticipation of the new AIFA document, however, unchanged problems still remain, the object and purpose of the research, linked to the introduction in the calls for tenders of original drugs and biosimilars competing with each other, a problem whose solution is crucial in programming, national and regional levels, the health economic measures, also inextricably linked to the use of appropriate and sustainable biosimilars.

Currently, without considering the administrative judicial appeals concluded or still pending, there is an absolute difference in treatment between the various Regions, such as the guarantee of the continuity of care, expected only in 10 Regions examined on 17 and in the remaining seven, only three foresee that the use of the originator ought to be justified by clinical motivation.

EFFECT OF BOVINE LACTOFERRIN ON INTESTINAL CELLS INFECTED WITH ADHERENT-INVASIVE *ESCHERICHIA COLI*

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Introduction. Adherent-Invasive *Escherichia coli* (AIEC) is a pathogen known to be involved in the Crohn's Disease (CD). A detailed study of the AIEC strain LF82 revealed that it is able to adhere to and to invade enterocytes, and to survive and replicate within human cells without causing death. Recently, bovine Lactoferrin (bLf), a cationic glycoprotein with antibiofilm, antibacterial and anti-inflammatory activities, was shown to be able to inhibit adhesion and internalization of facultative intracellular bacteria, including LF82.

Aim. This study is aimed at evaluating the effect of pretreatment of Caco-2 intestinal cells with bLf on the ability of this strain to invade and survive intracellularly as well as to understand the molecular mechanism involved.

Methods. Human epithelial colorectal adenocarcinoma cell line Caco-2 was differentiate for 15 days before infection. When required monolayers were pre-stimulated for 12h with bLf. To evaluate the invasion and intracellular survival of LF82, at the end of the treatment cell monolayers were lysed 4 and 24h post-infection. Moreover, we studied the ability of LF82 to induce apoptosis by fluorescence assay and to modulate the production of nitric oxide synthetase (NOS) and cytokines Interleukin (IL)-1β, 6 e 8 by ELISA test.

Results. LF82 is able to invade and survive in Caco-2 cells and bLf monolayers treatments reduced the invasion and intracellular survival of about 80% (p=<0.0001) and 45% (p=0.00009), respectively. In Caco-2 cell monolayers, pretreated with bLf and infected, the NOS levels were similar to untreated infected cells showing any bLf effect. The results obtained clearly demonstrated that apoptosis is not involved in the decrease of LF82 intracellular survival. For what it concern IL-1β and IL-6, our results indicate that bLf does not seem to have any influence on their modulation (infected or not), although IL-8 shows a significant increase in infected cells compared to noninfected cells (p=0.0001).

Conclusion. The results obtained suggest that bLf pretreatment induces a protective effect reducing the ability of LF82 to invade and survive intracellularly. Analyses of apoptosis and NOS production indicated that they are not involved in the mechanism of protection of bLf. Furthermore, the analysis of IL-1β and IL-6 indicated that their levels were not changed by the action of bLf between on cells pretreated or not. Studies are in progress to assay the effects of the bLf on autophagy.

EVALUATION OF A POSSIBLE URINE METABOTYPE IN PATIENTS AFFECTED BY *HELICOBACTER PYLORI*

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Introduction. Metabolomics is a field of study in systems biology involving the identification and quantification of metabolites present in a biological system. The analyses of metabolic differences between unperturbed and perturbed networks can provide insight into underlying disease pathology, prognosis and diagnosis. Metabolomics may also provide biomarkers useful for identification of early stage gastric pathologies. *Helicobacter pylori*, the human pathogenic gram-negative microaerophilic bacterium, causes chronic gastric infection in more than half of the human population. The presence of *H. pylori* can be seen as a results of the interaction between the system's genome with its environment and the organism's response, which can adapt itself, modifying his components, in particular proteins and metabolites in order to achieve a dynamic equilibrium. For this reason the variation of the concentration of such components in bloods and urines could be a systemic fingerprint of the presence of *H. pylori* and its consequent responses.

Objective. The aim of this study is the characterization of the urinary metabolic profile of individuals with Breath Test (BT) positivity to *H. pylori*. This study was carried out on 81 patients, 43 female and 38 male, between 35 and 70 years old. The group, afferent to the Endoscopy Center of IV Surgery Clinic of Umberto I Hospital, was divided in 3 classes: HP positive, HP negative and HP Resistant (BT positivity also after antibiotic therapy). A written informed consent was obtained from each subject before enrolment.

Methodology. The experimental protocol for the participation to this study consisted in taking, early in the morning, urine from patients afferent to the center. The samples (5 ml) were collected in appropriate containers with 0.05% of sodium azide and preserved at -80°C until analysis. At the same time anamnesis and clinical examination, including blood samples were collected. Urine samples were analysed by Nuclear Magnetic Risonance Spectrometer equipped with a 9.4 T magnet operating at a 1H frequency of 400.13MHz. 1H resonance assignment was achieved by standard 2D experiments (COSY, TOCSY, HSQC, HMBC and DOSY) on selected samples and confirmed by comparison with the literature, web and house database. To evaluate the differences in urine metabolic profiles of the group, multivariate and univariate analyses were applied. Principal component analysis (PCA) and Partial Least Square Discriminant analysis (PLS-DA) were applied as unsupervised and supervised data analysis, respectively.

Results. Urine NMR based metabolic profiles were obtained in relation to following variables: age, gender and BT positivity.

IMMIGRATION FEMALE: TRANSCULTURAL APPROACH AND SATISFACTION WITH NURSING CARE

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Cultural competence is a dynamic and ongoing process of learning. Understanding the evaluation process on cultural models and factors that influence individual and group differences is crucial in the prevention of generalizations and stereotypes to reduce disparities in access to health care. Healthcare providers are facing the need to develop intercultural skills that enable them to recognize their own cultural norms, understand the patient's point of view, and effectively adapt their behavior to maximize the cure. The quality of care, the nurse-patient relationship, as well as the satisfaction care and health outcomes improve when nurses and other professionals strive to understand the values, beliefs and ways of life of the assisted. This study aims to evaluate the cultural skills of nurses and patient satisfaction care received.

The literature search resulted in the selection of the following data collection tools for the purpose of the study:

- cultural Competence Assessment instrument (CCATool) - Italian version, evaluates the cultural competence of nurses;
- physician's Cultural Competence for Patient Satisfaction (PCCPS) - Italian version modified for nurses, satisfaction valuted about the nursing care patients.

Subsequently the relevant authorizations, have been areas identified within the ASL Roma 2 where it shall administering questionnaire. The patients involved have received nursing care at least two weeks prior to answer the questionnaire. The tools for patients and nurses are anonymous.

Preliminary results of the study on a sample of 20 adult patients and 36 nurses would seem to show at the time that 45% of nurses rated themselves as neither competent nor incompetent. The overall level of patient satisfaction care received is good.

It's necessary to complete the survey a larger number of participants that could indicate the change of the preliminary results.

IDENTIFICATION OF DELIVERY MODELS FOR THE PROVISION OF PREDICTIVE GENETIC TESTING: RESULTS OF A SYSTEMATIC REVIEW

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Background. Research on the integration of genomic knowledge into clinical practice and public health is in an early phase, and the appropriate application of genomic technologies in healthcare is surrounded by many questions. The aim of this study is therefore to identify, classify, and evaluate delivery models for the provision of predictive genetic testing in Europe *vs.* extra-European countries.

Methods. A systematic review of the literature was conducted to identify existing genetic service delivery models. Articles were retrieved through four electronic databases (Pubmed, ISI Web, Scopus and Google Scholar) using a common search strategy. Inclusion criteria were that articles be: published 2000-2015; in English or Italian; and from European or non-European countries (Canada, USA, Australia or New Zealand). Additional policy documents were retrieved from represented countries' government-affiliated websites.

Results. A total of 117 records were included, reporting on 149 genetic programmes delivered mostly in the United Kingdom (59, 39.86%), USA (35, 23.65%) or Australia (16, 10.81%). The programmes integrated into healthcare systems were 96 (64.43%), 49 (32.88%) were pilot programmes and 4 (2.69%) were direct-to-consumer (DTC) genetic services. Up to 130 (87.25%) genetic programmes were offered in the public sector, of which 8 (6.15%) were academic, 76 (58.46%) were community and 46 (35.38%) were both community and academic based. The main source of funding was public (93, 62.42%), followed by private and public funds (49, 32.88%) and only private funds (7, 4.70%). Tests for hereditary breast and ovarian cancer (61, 40.94%) and Lynch syndrome (23, 15.43%) were most commonly offered, followed by newborn screening panel (18, 12.08%), Familial Hypercholesterolemia (11, 7.38%) and Inherited Thrombophilia (5, 3.35%). A consent form prior to genetic testing was explicitly required and reported in 43 (28.86%) programmes. The identified genetic programmes can be classified into five genetic service delivery models based on which type of healthcare professional has the most prominent role in the model: I) the geneticists model; II) the primary care model; III) the medical specialists model; IV) the population screening programmes model; V) and the DTC model.

Conclusions. The present review, as part of a European multicenter study, will facilitate the identification of appropriate models for the provision of predictive genetic testing in Europe, in particular in the Italian setting. The review will also facilitate a rudimentary evaluation of the genetic programmes based on outcomes and process measures of the delivery models.

NEW PSYCHOACTIVE SUBSTANCES AND BIOMARKERS ANALYSIS BY LC-MS/MS AND UHPLC-HRMS

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Drug abuse is today a growing global problem that affects people of all ages. Often the consumers are not aware of what substances they are using and of the correlated risks. In recent years New Psychoactive Substances (NPS) are often sold as “legal-highs”: these substances are new molecules, natural or synthetic, which are sold in smart shops as incense, bath salts or standard not for human use, generally belong to definite chemical classes. The introduction of many new analogues designed to circumvent legislation is constant: whenever a new drug is scheduled, new analogues with minor modifications to the chemical structure appear on the market. NPS are therefore a high priority in the EU and many state members, including Italy. It is widely reported that the use of these substances is related with dissociate mental states and psychedelic sensations; however, because of the lack of legal restrictions to their marketing, these new drugs are easily available in the so-called “Smart Shops” or through e-commerce. These pharmacological effects and the difficulty in detecting the parent compound in urine highlight the importance of metabolite identification for developing analytical methods for clinical and forensic investigations. They are often extensively metabolized and excreted in urine, but for most of them limited human metabolism data are available. The major goal of our project is to develop and test innovative approaches for the detection of legal highs based on Liquid Chromatography coupled with Mass Spectrometry (LC-MS) or High Resolution Mass Spectrometry (LC-HRMS) using different approaches with suitable analytical and bioanalytical tools. We have developed different extraction techniques on samples of forensic toxicology interest such as blood, urine and hair, resulting in analytical tools with high sensitivity and specificity. These methods allow you to obtain qualitative and quantitative information on the analyzed NPS. In particular the High-Resolution Mass Spectrometry (HRMS) allowed the determination of psychoactive substances and identify their metabolites with high accuracy.

PERSONALIZED MEDICINE AND ADVERSE DRUG REACTIONS: AN ITALIAN EXPERIENCE

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The personalized medicine, emphasizing a clinical approach based on the uniqueness of each patient, has among its objectives to identify the preventive and/or therapeutic actions that best suits the needs of the single patient. It is known that a model of medicine aimed at the possibility of identifying the susceptibility of each person to possible diseases, measuring the risk, customizing the therapy according to the patient's genetic constitution and affecting the appropriateness of the drug administered, reduces the occurrence of adverse reactions. Nowadays, the term “adverse drug reaction” is identified with any harmful effect involuntary resulting from the use of a medicinal product; pharmacogenomics, in this field, has the aim to improve the drug response and to reduce the adverse reaction.

We analyzed all reports of adverse reaction collected in the Pharmacovigilance Centre database of an Italian University Hospital, at the Sant’Andrea Hospital Sapienza University of Rome, in a period of two years. Comparing the data result from our analysis with several studies found in literature, it’s evident that adverse drug reactions represent an important problem in the management of a health care system. However, the development of pharmacogenetics and pharmacogenomics, allowing a personalized treatment, can improve clinical practice. This study highlights the great potential of pharmacogenomics in reducing adverse reactions and suggests the need for further pharmacogenomic clinical trials to better personalize drug treatment and to refine the current pharmacovigilance strategies.

New research topics

LIFESTYLES AND QUALITY OF LIFE AMONG ITALIAN UNIVERSITY STUDENTS

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Introduction. Never has the importance of healthy lifestyles been greater than today. The age pyramid is shifting to an age dome and chronic diseases are steadily increasing, costing EU economies EUR 115 billion annually. Unhealthy diet, physical inactivity, tobacco and alcohol consumption cause an important part of chronic illnesses in Europe and are unfortunately very prevalent among young adults. University students represent an important subpopulation of young adults, who are subject to different kinds of stressors such as academic pressures and financial problems. The years spent at university are a crucial point of time and students are at a stage of live during which important lifestyle modifications, that subsequently influence their future health, take place. Previous studies have shown that unhealthy lifestyles among young adults are strongly linked to unhealthy habits in adulthood and an individual's Health-Related Quality of Life (HRQL). In respect of universities, promoting health means endorsing human development and effective learning. *Vice versa*, education is a significant predictor of quality of life and health. Identifying key areas of HRQL is therefore of great importance and can serve as an essential driver for health policy, health promotion and prevention programs.

Objective. In spite of the importance of students' health, and although information from several countries worldwide exists, data about Italian students' lifestyles and their HRQL is infrequent. Thus, the objective of the present study is to assess Italian university students' HRQL, including the Mental Composite Score (MCS) and Physical Composite Score (PCS), and to investigate the association of these scores with lifestyle habits.

Methods. The self-administered and online questionnaires were designed to measure student's lifestyle relating to smoking habits, alcohol consumption, dietary habits, physical activity patterns and HRQL. The questionnaires contain a sheet with demographic data, smoking prevalence, dietary habits, physical activity and the HRQL. The latter is measured using the SF-12 questionnaire; results will be used for calculating the MCS and PCS. Physical activity will be measured using the International Physical Activity Questionnaire (IPAQ). All data will be analysed using SPSS package 24.0.

Expected Results. Up to now, the sample consists of 1982 full-time university students from four different universities (Sapienza, Cattolica, Palermo, and Cassino). We hypothesize that healthy lifestyle habits and the health-related quality of life will differ between different age groups, universities and different study programs. All research activities are still on going.

ASSESSMENT OF BIVENTRICULAR FUNCTION IN HUMAN IMMUNODEFICIENCY VIRUS INFECTION BY THREE- DIMENSIONAL SPECKLE TRACKING ECHOCARDIOGRAPHY

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Purpose. The pathogenesis of Left Ventricular (LV) dysfunction in HIV patients includes cardiac direct effects of HIV, the presence of autoantibodies, myocardial inflammatory response to viruses, other infections related to the immune status of patients and side effects associated with antiretroviral drugs or other drugs used for the management of HIV. Three-Dimensional Speckle Tracking Echocardiography (3DSTE) makes it possible to detect a subclinical myocardial dysfunction at an early stage compared with conventional echocardiography.

Materials and methods. Patients with human immunodeficiency virus infection followed at our University Hospital and normal controls of the same age and sex will undergo a thorough cardiovascular evaluation. All patients will be stable in terms of HIV infection, with no history of heart disease or other chronic systemic disease except HIV infection. Patients will be on HAART with good immunological control, and will carry markers of inflammation, D-dimer, IL-6 and ultrasensitive PCR. Echocardiographic examinations will be performed with GE Vivid E9 equipment, and the data will be treated using special software. Three-dimensional data will be processed in a separate "workstation". Various apical and transverse scans will be obtained, and the end-diastolic and end- systolic volumes will be determined. The deformation parameters will be calculated using dedicated "software". The data will be analyzed on the basis of statistical analysis and logistic regression models.

Expected results. We expect that assessment of biventricular function by means of these new two-dimensional and three-dimensional parameters may improve the sensitivity of cardiac indexes in predicting a myocardial involvement in patients in HAART therapy. In most HIV-infected patients it was found normal left ventricular systolic function in studies conducted in the HAART era. LV ejection fraction has been shown to be in the normal range, and thus a single measurement of ejection fraction in asymptomatic HIV-infected patients cannot detect a subtle systolic dysfunction, which can be revealed with further investigation. In patients with HIV Right Ventricular (RV) impairment may also be shown, with signs of impaired systolic and diastolic function. The long-term prognostic value of systolic deformation parameters in HIV-infected patients should be evaluated in prospective studies. The recognition of a subclinical ventricular dysfunction may have the potential to address the anti-retroviral drug and cardiovascular therapies and influence the prognosis.

NEUROIMAGING OF PSYCOPATHY: CORRELATION BEETWEEN PCL-R AND MORPHO-FUNCTIONAL MRI

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In the last decades neuroimaging techniques have been broadly used to investigate neuropsychiatric disease. These techniques may be useful in delineating the neurobiology of psychopathy and in improving the knowledge of this disorder, even though many aspects remain unclear. Beside conventional morphologic MR sequences used in clinical routine to assess parenchymal alterations or structural brain disease, functional Magnetic Resonance Imaging (fMRI) have shown altered activation of brain regions during the resting state in several psychiatric disorders. Using several paradigms, measurement tools, and populations (both disordered and community), previous studies showed that individuals with high levels of psychopathic traits show lower activity in a number of affect-processing areas, in particular the amygdala and anterior insula and in regions typically associated with reward processing and cognitive control, including the ventral striatum and dorsolateral prefrontal cortex. These datas suggest that affective-interpersonal and lifestyle-antisocial facets of psychopathy may be associated with different patterns of atypical neural activity, which deserves future investigation. The aim of our project is to perform a multiparametric MR study in criminal psychopatic patient in order to evaluate morphologic changes in specific brain region involved in psychopatic disease and to assess eventually dysfunction in functional connectivity within the brain. This prospective study will include adult male subject (age > 18years old) recruited from a cohort of prison inmates with varying degrees of psychopathy. All subjects will undergo a neurocognitive and psychiatric evaluation. Imaging session with MRI examination will be performed on a 3T Siemens Verio Magnet. The exam will include morpho-structural sequences to evaluate the whole brain anatomy, volume and morphology of specific region involved in psychopathic disease including prefrontal cortex, temporal lobe, amygdala, striatus and hippocampus. These sequences will also be useful to investigate possible underlying pathology. We will also perform studes of brain activity using Brain Oxygenation Level Dependent (BOLD) functional sequences, that reveal changes in blood oxygenation and flow that occur in response to neural activity. These alterations in the local magnetic properties of the blood result in differences in BOLD signal intensity that can be measured to generate estimates of neural activity related to a particular psychological process. All data will be analyzed using dedicated algorithm and MRI structural and functional data will be correlated with clinical data in order to assess how morpho-functional changes in brain relates to the Hare's Psychopathy Checklist-Revised (PCL-r).

EFFECTS OF PROBIOTICS ON INTRATHECAL IMMUNE ACTIVATION AND NEUROCOGNITIVE PERFORMANCE IN ASYMPTOMATIC HIV INFECTED INDIVIDUALS

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Following the widespread of Highly Active Antiretroviral Therapy (HAART), the prevalence of severe neurocognitive impairment among HIV-infected individuals showed a significant decreased. On the other hand, the prevalence of milder extents of HIV-associated neurocognitive disorder, such as Asymptomatic Neurocognitive Impairment, remains elevated among this population. In several studies, Neopterin has been found in elevated concentrations in the cerebrospinal fluid of HIV infected subjects and its currently considered to be a useful biomarker of central nervous system immune activation among this population. Data from literature showed that modifications in microbiota composition, such as a reduction in Bifidobacteria, Lactobacilli or Bacteroides, commonly observed among HIV positive population, might be associated with an increase in systemic immune activation markers expression and with the onset of behavioral and neurocognitive alterations. According to the WHO definition, probiotics are "live microorganisms which upon ingestion in sufficient concentrations can exert health benefits to the host"; the use of probiotics among HIV infected individuals has already been proven to decrease intestinal intra-epithelial inflammation and to reduce the systemic expression of immune activation markers. Although studies focusing on the HIV infected population are lacking, novel data suggest that the administration of probiotics might exert beneficial effects in neurocognitive health in several pathological settings. Supplementation of HAART with probiotics could represent a novel approach for the prevention and the management of neurocognitive involvement during the course of HIV infection.

Aim of the present study is to evaluate whether supplementation with probiotics in HIV infected individuals presenting with neurocognitive impairment exerts an ameliorative effect reverting or delaying the progression to a more severe involvement. Secondarily, we aim to assess the effect of probiotics on central nervous system inflammation status and to evaluate the existing interrelation between central inflammation and neurocognitive performance. Given the available scientific evidences, we expect to observe a reduction in neuroinflammatory markers and an amelioration in participants' neurocognitive performance after probiotic supplementation. Our results could provide new insights on the microbiota-gut-brain axis of HIV positive subjects and suggest a novel way to manage neurocognitive involvement among this population.

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

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The head trauma and hypoxic-ischemic encephalic injuries are a major cause of death whose framework are taken into account the neurological characteristics and the changes identified with CT and MRI.

Our study research evidence about the correlation between genetic variants, extent of brain injury and clinical outcome after TBI. In the literature it was demonstrated the existence of a fairly precise chronology of expression of different markers of cerebral hypoxic-ischemic injury due to a stimulation of different cell types and to a different response from the ischemic insult cells. Oxidative stress plays a major role in the genesis of delayed adverse effects that contribute to permanent damage.

An important area of research is the identification of the period of hypoxic-ischemic injury to the assessment of the causal link and any responsibilities with the methodological rigor of their discipline, articulated by means of: - an examination of the medical records and imaging studies; - *pre-post mortem* radiological study; - Autopsy complete with biological samples; - complete histological investigation. An autopsy is the Prince survey and its value is enhanced with the help of appropriate toxicological investigations, microbiological, genetic and histological. Particular attention should be paid to the research of cell changes after the hypoxic-ischemic and whose precise history is well known in the literature. Upon completion of the routine histopathological reading, using new immunohistochemical type searches for the detection of proteins or enzymes expressed at brain level in subsequent stages to a traumatic event / hypoxic-ischemic. In order to find reliable markers, objective and repeatable, which anchor the judgment on the age verification pathological insult, we will proceed to the review of a large series of autopsy surveys conducted at the Institutes of the Universities and Research Centers.

The brain samples represented by cortical levies, basal ganglia and brainstem, will be sectioned and stained with hematoxylin-eosin accompanied by argentic, Perls and Von Kossa. For the next immunohistochemistry will be used an antibody panel based on the most recent scientific literature on the subject of damage brain, directed against: GFAP, TNF, IL1, IL-6, MAC387, HSP 27, 70 and 90, COX2, ORP150, b-APP, Tryph, GAP-43, apoptosis (TUNEL-TdT enzyme). The application of this methodology would allow to identify immunohistochemical markers for evaluating the timing of brain damage.

CARDIO METABOLIC RISK IN THE BUILDING SECTOR

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The cardiovascular diseases are one of the most important public health problems in industrialized countries. The literature shows a high prevalence of cardiovascular risk among construction workers and reveals how the main occupational risk factors such as noise, dust, fibers, manual handling of loads, prolonged static positions, repetitive movements, hand-shoulder vibration and whole body, products chemical and weather conditions combined with the non-occupational risk factors such luxuries habits and lifestyle can significantly affect health with alterations in organs and systems. Important precursors of cardiovascular disease among the construction workers are obesity, hypertension, and abnormal lipid profile caused largely by a harmful lifestyle such as unhealthy diet, insufficient physical activity, and habit of cigarette smoking and alcohol. The risk assessment cardiometabolic workers in the construction industry is the need to reduce occupational and no-occupational risk factors that determine the onset of cardiovascular disease and promote the need for healthy lifestyle programs and health awareness in the workplace.

It will be considered an initial representative sample of at least 20 companies operating in the construction sector with a minimum of 10 workers assigned to different types of tasks divided as follows: driver, laborer, electrician. All workers included in the study will be evaluated annually during a medical health surveillance required pursuant to Legislative Decree 81/08 and s.m.i. For every worker will be collected clinical and medical information about work history, physiological anamnesis, recent and remote medical history and pharmacological history.

During the visits will be assessed the following cardiometabolic risk factors: waist circumference, body mass index, fasting glucose or diabetes medication, cholesterol or specific therapy, blood pressure or antihypertensive therapy and ankle-brachial index.

Quantitative data will be analyzed using SPSS statistical software. To exclude the influence of the main factors confounding the multiple linear regression analysis will be performed using as independent variables age, sex, length of service, alcoholic habits and smoking habits. The associations between heart disease and occupational risks will identify the employment aspects on which action to improve not only productivity and organizational well-being at work but also the quality of life and health of the worker. It will also be possible to recognize the predictive value of parameters such as waist circumference, body mass index blood pressure and ankle-brachial index that will not affect the costs of the company.

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

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Anisakis is a parasitic nematode which infects marine fish and can cause gastrointestinal disease if accidentally ingested. Infection can be accompanied by IgE mediated hypersensitivity reactions such as urticaria, angio-oedema and anaphylaxis.

The Scientific Opinion on risk assessment of parasites in fishery products recognizes that the only parasite potentially present in fishery products, which is implicated in allergy, is *Anisakis simplex* and the sensitisation occurs via infection by live larvae. However, workers involved in fish processing can develop allergy to *Anisakis* and a potential occupational risk was suggested: in fishermen and workers assigned to fish processing and sale, indeed, have been described occupational allergy to *Anisakis*, including asthma, rhinoconjunctivitis and protein contact dermatitis. Further researches are needed on the prevalence and mechanism of disease. EFSA recommends coordinated studies to improve surveillance and diagnostic awareness of allergic reactions to parasites in fishery products. The *in vivo* (skin-prick tests) and/or *in vitro* level of specific IgE, are usually used for diagnosis of sensitization to the parasite, and it is accepted that these tests are highly sensitive methods. *Anisakis* proteins demonstrate considerable immunological cross-reactivity to proteins of related nematodes and other invertebrates such as house-dust mites and cockroaches, probably responsible for false-positive results. Specific IgE to allergens from the parasite can be also detected by immunoblotting (WB) which is a method more specific. Furthermore, in the last years extensive data support the use of the Basophil Activation Test (BAT) in allergy diagnostic investigations, using flow cytometry analysis. The BAT should be considered as a third level diagnostic aid and requires professional competence.

The aims of the present study are: a) to evaluate the prevalence of *Anisakis* sensitization in the occupational setting; b) to apply more specific diagnostic tests; c) to compare the performance of the analytical methods; d) to elucidate potential exposure pathways and suggest possible prevention strategies. The expected results will be: a) to increase knowledge on the prevalence in specific risk categories; b) to highlight the working conditions at increased risk of exposure (individual and collective) c) to evaluate the results of the application of more specific analytical tests for the *Anisakis* allergy diagnosis.

POLICY ANALYSIS FOR THE PROMOTION AND PROTECTION OF THE HEALTH OF IMMIGRANTS IN ITALY

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The immigration phenomenon, with its complexity, represents one of the most challenging changes that Italians have had to face during the last twenty-five years. Although the immigration policies are governed centrally, the reception, integration and health promotion activities and the social care of migrants take place at local level, in each Region. In recent years, the political and administrative decentralization has resulted in a considerable heterogeneity in guaranteeing equity of access to standard healthcare provision to migrants, and this has depended mainly on the difference in sensitivity and attention given to the issues of right to health and social inclusion by local authorities. Different factors, interacting with each other, have strongly influenced the situation, which was further aggravated by the current socioeconomic crisis. This has resulted in the rationalization of the regional health systems due to the budgetary constraints imposed by the financial Recovery Plan and has included the introduction of specific measures like tickets for services and pharmaceuticals. In addition, the migration phenomena, despite having assumed over time a character of stability, can present dynamic and unexpected implications, both on a quantitative and qualitative level. For example, with regard to the phenomenon of refugees arriving on the Italian coasts in recent years (more than 181,000 in 2016), it is hard to find a valid strategy to intercept, receive and include these people in the national protection systems, including the health care system. Migrants in Italy are a "fuzzy" set and it is difficult to apply to them a dichotomous categorization in terms of classification. Furthermore, the epidemiological profile of such a heterogeneous population varies according to the influence that various determinants have had on their health during the migration process. Therefore, the need emerges for a more coordinated action at national level to preserve and extend public health universalistic policies and to translate them into effective service accessibility. To promote a real governance of the phenomenon, it is essential that organizational decisions in the health and social sector are accurately monitored in order to evaluate the impact that these decisions have on the health conditions of migrants. The goal of this research is to provide a basis of information useful for the production of recommendations and guidelines on organizational models and best practices that can be implemented in various regional/local contexts, and, ultimately, to the development of highly inclusive and evidence-based public policies based on Health Impact Assessment (HIA). Its overall objective is to improve the knowledge of appropriate current data on the access to health services by immigrants.

COST ANALYSIS OF HEALTH CARE-ACQUIRED INFECTIONS IN A TEACHING HOSPITAL IN ROME: A COMPARISON OF METHODS

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Healthcare Acquired Infections (HAIs) are an important cause of morbidity and mortality in hospitals, where about 5-10% of patients are affected, determining high associated mortality, and adding costs. The European Centre for Disease Prevention and Control (ECDC) calculated that annually HAIs involve about 4.1 million patients in all the European Union. In order to estimate the cost of HAIs several studies have been carried out worldwide. However, quantifying exactly the economic burden still remains a challenging issue.

Appropriate methods are important in the analysis to determine associated extra costs; uneven methodologies have produced significant variation in cost estimates because of variation in sample size, hospital ward characteristics, infection sources, economic model, and case finding methods. Overall it is difficult to evaluate all variables exactly implicated, especially indirect costs (patient's lost of salary, diminished worker productivity, income lost by family member), therefore, investigators generally estimate only direct additional costs and, particularly, additional Length Of Stay (LOS), which represents the single most relevant expensive element.

There are several methods to estimate extra LOS. The first to be used was a highly subjective method, represented by "self physician assessment". Later, three other objective methods were widely adopted, unmatched group comparison, matched control comparison and the Appropriateness Evaluation Protocol (AEP) based methodology. Some of them flawed to distinguish accurately between the type and amount of resources specifically associated with treating HAIs and those incurred for the principal clinical cause for which the patient was admitted and used average total cost.

The aim of this study is to compare the methods internationally used for estimating days of hospitalization attributable to hospital infections by applying them to the same population. The study will be carried out in the teaching hospital Sant'Andrea in Rome. An increase in costs management of patients suffering from HAIs is expected. This increase will depend to the type of infection and the inpatient ward. It will be possible to distinguish between treatment required for HAIs and treatment due to the main clinical problem. Determining the cost of nosocomial infections can help to establish priorities for implementation of measures or programs designed to reduce the incidence of these infections in the different healthcare organizations and provide better support for the decision making process in infection control.

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

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The aim of the present qualitative study is to explore and understand the self-care process in women with a diagnosis of breast cancer. Breast Cancer in women have different aspects related to the person. Many problems are linked with the ability of the individual to self-care (the ability of individuals, families and communities to promote health, prevent disease, and maintain health and to cope with illness and disability with or without the support of a health-care provider), this is an important health care issue for nursing as well as public health. This study will use an exploratory qualitative design through Grounded theory methodology. Women with breast cancer diagnosis with or without mastectomy who have different experiences of self- care related to age, marital status, education, socio - economic status, employment status, duration and severity of disease will participated in study. Sample size will be determined by data saturation. Interview will consist of a single question related to the process of self-care.

Data will be analyzed manually at the first step and by MAXQDA software (Version 10). Process of collecting and analyzing data will be concurrently performed. Analyzing data will be carried out following Corbin and Strauss process and Grounded Research methodology approach (2008). Being a qualitative study, different tools of analysis will be used in order to give meaning to the themes.

Constant comparison and theoretical comparison of the different meanings will be taken into consideration enriching the value with deep concepts *restitution* when necessary. At the end a theoretical model of self-care process in women experiencing breast cancer will be provided.

The results of this study should hopefully be used to formulate standard of care and policy in our country for the benefit of breast cancer women and their families.

ROLE OF VIRAL INFECTIONS IN DETERMINING EPIGENETIC AGING

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Chronological aging is a natural process characterized by time-dependent deterioration of multiple biological and cellular functions. It is known that complex molecular changes, including epigenetic modifications, are hallmarks of aging. Both histones modifications and DNA age-related hypo- and hypermethylation have long been observed in various species and recent studies showed that DNA methylation level correlates with chronological age in non-pathological conditions. Furthermore, these modifications can be used as an index of aging called "Epigenetic Age", also known as DNA methylation Age (DNAm Age), that predicts age by analysing CpGs methylation levels. Interestingly, it has been recently shown that Epigenetic Age may increases in numerous human age-related pathological conditions, such as Alzheimer's Disease (AD).

In the last decades, it has been demonstrated that infectious agents interact with the cells genome by modulating host epigenetic machinery. For example, herpesviruses undergo methylation of viral DNA, but are able to counteract this process through viral proteins, thus allowing the correct life cycle in host cells, and likely affecting host epigenetic balance. Although the consequence of virus infections in host aging are not completely understood, growing evidence suggest that viral infections may promote cellular decline. Besides, several papers show evidence supporting a potential relationship between viruses (e.g., Herpes simplex virus 1, HSV-1; Epstein-Barr virus, EBV; Influenza A virus, IAV) and various diseases affecting central nervous system (CNS). In particular, previous works from our group showed how HSV-1 infections in neurons play a pivotal role in the appearance of the main neurodegenerative hallmarks that characterize AD; they also demonstrated that HSV-1 productive infection in neurons causes DNA damage and affects cellular repair systems, both hallmarks of aging. Thus, this study is aimed at characterizing the interplay between viruses, particularly HSV-1, and Epigenetic aging, particularly of CNS.

This aim will be achieved by: a) evaluating the levels of aging hallmarks, such as post-translational modifications of histones (e.g., H3K56ac, H4K16ac) and CpGs methylation levels in *in vitro* and *in vivo* experimental models of acute and recurrent virus infection (e.g., cell lines, primary cultures of rodents neurons, primary co-culture of neuron/glia cells, mouse); b) analysing viral proteins and cellular pathways involved in virus-induced epigenetic alterations.

EFFECT OF INTERFERON FREE ANTIVIRAL THERAPY ON GLOMERULAR AND TUBULAR KIDNEY INVOLVEMENT IN HCV CHILD-A CIRRHOSIS

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Hepatitis C Virus (HCV) infection is associated with an increased risk of renal disease. Patients with chronic hepatitis C have a greater risk of developing Chronic Kidney Disease (CKD) compared to uninfected individuals with a prevalence ranging between 5% and 18% and a faster decline of renal function.

The correlation between HCV infection and glomerular damage is well recognized, conversely HCV-mediated tubular damage is an unclear debated issue and has not been clearly understood. The presence of HCV antigens and viral RNA has been demonstrated by histological examination in tubular epithelial cells of renal biopsies of HCV infected patients, but the presence of tubular involvement has never been studied *in vivo* in HCV infected patients. Recently, several novel Direct Antiviral Agents (DAAs) have been approved for HCV treatment, with impressive cure rates, higher than 90%, after 8-12 weeks of therapy and mild adverse events. The effects of HCV clearance on renal involvement has not been fully characterized.

The aim of this study was to evaluate the effect of viral eradication, by means of DAAs, on renal Glomerular (GI) and Tubular Involvement (TI) in patients with HCV-related cirrhosis. We enrolled Child-Pugh A cirrhotic patients treated with DAAs attending the outpatient Infectious and Tropical Disease Clinic at Umberto I hospital in Rome. Demographic, clinical, biochemical and virological characteristics of enrolled subjects were collected. The diagnosis of liver cirrhosis was performed by biopsy and/or Transient Elastography. Estimated Glomerular Filtration Rate (eGFR) assessed by CKD-EPI 2009 equation, urinary Albumin-to-Creatinine Ratio (ACR), urinary alpha1-Microglobulin-to-Creatinine Ratio (α1MCR) and sodium fractional excretion (FeNa) were evaluated before starting therapy (T0) and six months after treatment withdrawal (FU6). Renal function, evalueted by eGFR, was defined according to KDIGO classification. Glomerular involvement was defined as ACR>30µg/mg, tubular involvement was defined as α1MCR>14µg/mg and/or FeNa>1.

Preliminary data confirm the presence of glomerular involvement and identifies for the first time the presence of tubular involvement in HCV cirrhotic patients. A significant improvement of either non-diabetic glomerular either tubular HCV-induced damage occurred after HCV clearance by DAAs therapy. However, glomerular involvement did not resolve in diabetic HCV patients after treatment, since in these subjects glomerular kidney damage could be mainly driven by the metabolic disorder rather than by HCV infection itself. These results seems to confirm the strong relationship between HCV infection and kidney glomerular and tubular involvement and underline the importance of antiviral treatment.

ROLE OF ERYTHROCYTE MEMBRANE MICRODOMAINS IN *PLASMODIUM FALCIPARUM* INFECTION

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Malaria is the deadliest parasitosis worldwide, causing 214 milion cases and 438,000 casualities in 2015. Among the members of *Plasmodium* genus, *Plasmodium falciparum* is the main cause of death in humans. The identification of new antimalarial drug targets is a fundamental challenge, given the continuous emergence of drug-resistant strains of *P. falciparum* in endemic areas.

Membrane Microdomains (MMs) are specialized regions of the cell membrane with distinct protein and lipid composition, involved in several biological processes, including signal transduction and intracellular pathogen infection. Disruption of MMs in human Red Blood Cells (RBCs) prevents infection by *P. falciparum*.

In a proteomic analysis carried out in the laboratory led by Marta Ponzi, 158 proteins were identified in MMs from human RBCs. These proteins were clustered by their floating profile in the sucrose gradient used to purify them, obtaining 12 groups. Each of these groups is expected to contain proteins associated to the same MM subtype.

To date, 11 erythrocyte proteins are known to be involved in *P. falciparum* invasion. Among them, 8 were identified in MMs and 6 fall in the same cluster, that includes 15 proteins. This result suggests that *P. falciparum* invasion could be dependent on a single MM subtype. As a consequence**,** the proteins identified in the invasion cluster become extremely promising, being potentially involved in *P. falciparum* infection. Most of these proteins are involved in signal transduction, suggesting that parasites exploit the host signal transduction cascade to invade.

The main goal of this project is to charachterize the functional role of the candidate proteins emerged from erythrocyte MM analysis in relation to malaria infection, in order to identify new pharmacological targets. This goal will be pursued with different approaches. To assess the contribution of each candidate protein to the infection process, erythrocytes will be treated with chemical inhibitors or with monoclonal antibodies directed to the candidate proteins and then infected with *P. falciparum*. Invasion rates will be measured by FACS analysis. We'll also describe the subcellular localization of each candidate protein by immunofluorescence assays during *P. falciparum* invasion at different time points in order to analyse each phase of the process. Furthermore, in order to define molecular interactions of each candidate protein during invasion, we'll perform co-immunoprecipitation experimentos (Co-IPs) with antibodies specific for each candidate protein. Once identified the interacting partners, we'll repeat Co-IPs with antibodies directed to them, in order to confirm interactions and possibly identify other proteins involved in the invasion process.

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

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Myocardial Infarction (MI) is a major cause of mortality and disability in the world and represents an outcome measure in quality programs in health systems.

In the clinical practice, the diagnosis of early stages of myocardial ischemia, within 6-8 hours ischemic insult, in which they are not yet clear histomorphological signs, it remains an unsolved problem. The goal of this research is to detect and quantify the expression of miR-1, miR-133a, miR-499 and miR-208a on cardiac tissue samples from subjects who died of MI, in the first 6 hours of the onset of clinical symptoms, attributable to myocardial ischemia. The casistic will be selected from autoptic cases of the Section of Pathology Forensic University of Foggia, characterized by a clinic and *post mortem* setting (symptoms, ECG, laboratory) indicative of MI. It will set up a control group composed of an equal number of subjects whose death was not due to MI.

For each case, we will study the cardiac tissue samples (7 standard samples), collected in the course of autopsy and preserved in formalin, on which will be made the dosages of miRNAs mentioned above.

The expected results and prospects of the study are to:

- verify the significant difference for qualitative and quantitative expression of the studied miRNAs, between the group of subjects with early MI and the control group;
- compare the qualitative and quantitative expression data of miRNAs with clinical and autopsy findings of patients with MI, in order to evaluate the expression pattern of miRNAs investigated at 0,1,3 and 6 hours by the ischemic myocardial injury;
- on the basis of such data, process a chronological table for the early determination of MI, in the period of time between 0 and 6 hours after myocardial ischemia;
- implement the diagnostic capability of early MI for the forensic pathologist and arrive at a more exact dating of early MI (0-6 hours by the ischemic myocardial injury) responding, thus, for a precise forensic requirement;
- providing to clinical research, valuable information on the pathophysiology of the early phases of MI, helping thus to better understand the underlying pathophysiological mechanisms and to suggest targets for future therapies.

PROBIOTICS MODULATE TOLL LIKE RECEPTORS, TYPE I/III INTERFERON AND RETROVIRAL RESTRICTION FACTORS IN HIV-1 INFECTED PATIENTS

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The disruption of mucosal integrity in the gut is the major cause of persistent immune activation during chronic HIV-1 infection. Recent findings support the clinical benefits of probiotics during HIV-1 infection trough the reduction of intestinal permeability and, consequently, microbial translocation. In this regard, it is known that recognition of PAMPs by pathogen-recognition receptors in the gut, such as the family of TLRs, and in particular TLR4 and TLR9, triggers intracellular signaling cascades ultimately culminating in the activation of the type I and III IFN response. Given that type I IFN has detrimental effects during HIV-1 infection and that IFNlambda seems to play a significant antiviral activity in the gut site, the expression of TLR4/9, IFN alpha/lambda subtypes, and some IFN induce restriction factors will be evaluated both in gut and PBMC of ART treated HIV-1 patients. Moreover, the probiotics effects on IFN-mediated immunity will be also analyzed.

The aim of the study is to analyze ten HIV-infected subjects with stable suppression of viral load who will undergo endoscopic procedures and blood collection prior to initiation of probiotics supplementation (T0) and after 6 months (T6). Mucosa biopsies will be obtained and lamina propria lymphocytes will be isolated. TLRs, IFNalpha (n=12) and IFNlambda (n=3) subtypes, SAMHD1, Mx2, APOBEC3G and IFI16 will be measured by RT/ real-time PCR.

We are expecting a modification in the expression profile of IFN and/or IFN-related pathways after probiotic supplementation: in regard to the IFN species/subtypes and retroviral restriction factors analyzed, we are attending a differential modulation both in gut and PBMC at T6. Finally, we are predicting a positive correlation between some immune activation markers and IFN species/subtypes and retroviral restriction factors before probiotic supplementation both in gut and PBMC.

This study will provide the first evidence that TLR, IFNalpha and IFNlambda subtypes, and restriction factors are differentially expressed in the GALT and PBMC of HIV-1-infected patients and that the probiotics supplementation is able to change the expression of some IFN subtypes and IFN-related pathways, highlighting the important role of gut microbiome composition in regulating the innate antiviral response and providing the basis for a well executed large clinical trial.

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

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Since 2008 in Italy developed a series of reforms regarding security measures, with the abolition of judicial psychiatric hospitals (OPG) for persons Non-Guilty in Reason of Insanity (NGRI). People NGRI and considered socially dangerous, are now detained in the residential forensic units called R.E.M.S (Residences for Execution of Security Measures).

Violent behavior sometimes occurs in Schizophrenia and Mood Disorder, often in acute phases. Violence is also very common in about 80% of people with Borderline and Antisocial Personality Disorder. It's not clear why 35% of Psychosis begin with violent behavior. Clinical literature shows that Duration of Untreated Psychosis (DUP), has an important role in predicting aggressiveness during the first psychotic episode. At the same way, literature show that Personality Disorder (Borderline or Antisocial) in comorbidity with drugs abuse and psychopathy correlate with severe violence in criminal sample.

Psychopathy describes individuals who suffer from a profound affective deficit, including shallow emotion and inability to experience empathy, guilt or remorse. These behavioral deficits are believed to predispose psychopaths to high rates of criminal transgression and recidivism.

Research has identified several environmental, psychological, and social pathways that potentially lead to this personality development. We developed a protocol in order to measure both psychological and biological variables in psychopathic persons who have been evaluated NGRI and we evaluate the association with recidivism.

Case and Control are adults male, recruited in the REMS of ASL Rm5. All subjects will undergo a neurocognitive and psychiatric evaluation, severity of psychopathy will be assessed with the PCL-r. For group analyses participants will classified as psychopathic if their PCL-r scores will be $\geq$30 and non-psychopathic if their PCL-R scores will be $\leq$20.

Clinical assessments and PCL-r scores is going to be compared with neuroimaging acquired with Magnetic Resonance (MR) specific sequences in order to evaluate brain morphology and dysfunctional in connectivity and cognitive measures.

HUMAN ENHANCEMENT, THE NEED FOR SHARED APPROACH

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The concept of human enhancement is based on techniques which improve knowledge, to transform the aesthetic aspect, to increase physical and sportive performance, and increment the capacity for work. With the progress in science and biomedical technology especially in the settings of neuro science, genetics, bio- cyber technology, which affect the human biology improving the characteristics, we found themselves far from the traditional methods based on the "cure" and "prevention" of the diseases. The biojuridical debate, team doctor and of public health is made complex in attempting to codify the rules. Human Enhancement is facing a globalized "phenomenon", in which the departure condition is the "state of integrity", then every risk related to a medical act appears as a principle ethically not justifiable. The Science and Technology Options Assessment Committee has divided the HE in five areas: Emotional Enhancement, Cognitive Enhancement, Physical Enhancement: Life-Extension; Selecting the Best Children.

Through a first phase of framing by means of terminological analysis and an evolutionary historical dissertation of concepts of health and strengthening, addressing the aspects of biojuridical pertinence, a second phase of detailed analysis of Italian and European regulatory framework and literature review, and a third and last phase of analyzing a sample of selected individuals who were submitted for HE treatment, the objective is to analyze the HE phenomenon under a normative profile, the impact on the scientific community, and to experience interpretative hypothesis.

The hypothesis of a "case by case" approach, ductile and is able to allow in due account the truly peculiar characteristics of each form of strengthening, different from each other, with the possibility of adopting different solutions according to the specificity, will be verified with respect to a simplifying perspective of standardized and universal procedures (see guidelines / protocol) of the regulation of the matter.

A systematic research which is read and interpreted in a selectively juridical perspective and a proposal of regulation would allow the gathering and ordering of the complexity of knowledge and the structuring in key of possible clear solutions and of easy applicability. Under the journalistic profile the study offers the opportunity to develop a line of productive research of possible outcomes to be accredited on National and International magazines. The perspective of European comparison enriches finally in terms of originality and editorial opportunities.

CREATION OF A PREVENTIVE MEDICINE CENTER AND HEALTH CARE SERVICE FOR MEDICAL STUDENTS OF “SAPIENZA” UNIVERSITY OF ROME: A PILOT PROJECT

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“Sapienza" University of Rome is the largest University in Europe, welcoming students from all Italian cities and everywhere. Focus of this project is on 3504 students of the Faculty in Medicine, considered the most exposed in their technical and practical activities. About 60% of these students are out of their home and city and not rarely they deal with many difficulties especially because the independent management of their own health (hence the loss of contact with their family physician). Often these subjects begin with unhealthy lifestyle habits such as smoking or increasing in the average cigarettes consumption, unhealthy dietary habits as well as issues concerning the biological risk related to their training. All these aspects, where are coincident, act synergistically as a source of stress influencing negatively on academic studies, on health and on quality of life.

Aims. The project provides the establishment of a pilot center of preventive medicine and health care that can contribute in protecting health and the quality of life of these students. There will be: a) a department of Preventive Medicine with expertise in vaccinations for health workers and lifestyles (some questionnaire will be administered for lifestyles monitoring such as the "food frequency questionnaire", “IPAQ” and “SF36”); b) a General Medicine Service; c) the creation of a website dedicated to these issues.

Expected results. From a preliminary investigation based on questionnaires, it resulted that non-resident students have more difficulties to contact their Family Physician and are therefore more interested in the use of the service. With the beginning of the University, male students start to smoke and they engage in unhealthy lifestyles (worsening in eating habits and reducing in physical activity). Our work aims at improving the students lifestyle beginning to “Sapienza” University. With the implementation of monitoring programs about dietary and physical education, we expect a significant improvement in healthy lifestyles and quality of life.

CONTRIBUTION OF ASTHMA IN OPIATE DEATHS

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Although some studies have shown a link between asthma deaths and opiate abuse, the process in which opiates exacerbate asthma is still unclear. Opiates may impair judgment during an acute asthma attack, leading to inadequate treatment. Alterations in mental status may increase aspiration risk. Some studies have also demonstrated an opiate-induced bronchoconstriction.

In our country, according to the 2015 Annual Report of the Central Directorate for Anti-Drug Services, heroin was the drug that caused the greatest number of deaths, among the drug abuse deaths. The prevalence of asthma in Italy, according to the Italian Statistical Yearbook of 2015 (ISTAT), accounted for the 5.6% of the total population.

This study has the aim to provide data on opiate deaths in the Department of Forensic Medicine of Sapienza - University of Rome and in Cook County Medical Examiner's Office in Chicago (USA) and to compare the demographic, anamnestic, seasonal, autopsy, histological and toxicological findings of opiate users who had a history of asthma with those who did not. A histological grading of asthma changes is performed.

At the end of the study, the rate of clinical history of asthma in deaths due to opiates, as well as demographic data and seasonal patterns will be evaluated. Statistical analyses will be performed to compare the toxicological levels of opiates in asthmatic and non asthmatic, to infer the role of asthma in these deaths, also considering the different histological grades of asthma.

Our preliminary data (855 cases of opiate deaths) showed that a history of asthma can be present in opiate deaths (it accounted for the 9.12% -78 cases). The majority of people who died of opiate intoxication and had a history of asthma were males and African-American. Deaths usually occurred in winter and in spring, probably because cold air and pollens act as a trigger for exacerbations of asthma, together with the drug. In asthma cases, the level of morphine in blood ranged between 23-1,740 ng/ml (Mean: 209.51 ng/ml), the level of blood 6-MAM ranged between 12-280 ng/ml (Mean: 80.6 ng/ml) and the level of blood codeine ranged between 24-34 ng/ml (Mean: 26.6 ng/ml). In our cases with a history of asthma where the route of administration of the drug was inhalation, the grade of asthma was mild: this can support the hypothesis that inhalation, affecting lung tissue more directly than injection, can lead to death even if preexisting asthma changes are minor.

GUT MICROBIOTA IN PATIENTS WITH NEURODEGENERATIVE DISEASES: INFLUENCE OF MEDITERRANEAN DIET AND VITAMIN D

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Gut microbiota works as a true "metabolic organ", interacting with human host and developing essential functions; the condition in which the structure and composition of microbial population result altered (dysbiosis) it has been related to several pathologies. Regard phisiologic interaction between gut and brain, it has been proposed by some Authors that intestinal dysbiosis could be a basal state enhancing misfolding and prionic-like diffusion of aberrant proteins characterizing neurodegenerative diseases.

How is emerging in last years, in Alzheimer's disease, protein beta-amyloid appear to be part of a innate-immunity mechanism against microorganisms and/or microbial structural molecules. Furthermore it has been demonstrated that an unbalanced diet towards animal-derived proteins and fats, as well as refined sugar and flour is able to select a dysbiotic gut flora with consequent reduction of neurotransmitters production (95% of serotonine is gut-derived).

The present project is aimed at evaluating the influence of Mediterranean diet and vitamin D consumption on the composition of fecal microbiota and inflammatory parameters, in patients with neurodegenerative diseases (PD and/or AD), at different stages, following the progression of the disease.

In particular, our purpose is to evaluate whether a correlation exists among dietary habits, including vitamin D intake, fecal microbiota composition obtained with Next Generation Sequencing (NGS), intestinal permeability status (through evaluation of tight junctions protein zonulin), measurement of peripheral LPS, vitamin D value and immunological parameters (circulating cytokines) and clinical markers of disease severity and progression as concentration of aberrant protein beta-amyloid for Alzheimer's disease and alpha-syn for Parkinson's disease.

Subsequently a group of patients will voluntarily follow Mediterranean diet supplemented with vitamin D and probiotics.

The results obtained might add knowledge to the hypothesis that Mediterranean diet, ipocaloric and rich in anti inflammatory components, by decreasing dysbiosis and gut inflammation, might play a protective role in neurological neurodegenerative disorders.

Session 2

Infectious diseases, microbiology and parasitology

Chairpersons:

Cecilia Ambrosini, Miriam Lichtner, Marco Pombi

MULTI-DRUG RESISTANT *KLEBSIELLA PNEUMONIAE* STRAINS CIRCULATING IN HOSPITAL SETTING: WHOLE-GENOME SEQUENCING AND BAYESIAN PHYLOGENETIC ANALYSIS FOR OUTBREAK INVESTIGATIONS

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Carbapenems resistant Enterobacteriaceae infections are increasing worldwide, representing an emerging public health problem. Phylogenetic and phylodynamic tools applied to bacterial whole genome and core SNPs analysis have become essential in the epidemiological surveillance of multi-drug resistant pathogens circulating in hospital settings. In this study, between January 2012 and February 2013, twenty-one *K. pneumoniae* multi-drug resistant strains, circulating within different wards of the University Hospital Campus Bio-Medico, were collected and whole-genome sequenced. Classical epidemiological data and Bayesian analysis of high-resolution whole-genome sequencing were combined to evaluate the time-scaled phylogeny and the phylogeography of the microorganisms in support of hospital infection control. Genomic DNA from isolates was then sequenced on the Illumina MiSeq platform. Paired-end 250 base-pair reads were mapped to the *Klebsiella pneumoniae* strain CAV1596 reference genome, and high-quality single-nucleotide polymorphisms (hqSNPs) were called using an established bioinformatics pipeline in Galaxy. These hqSNPs were based on the core genome shared by all isolates, i.e. regions in the accessory genome not conserved by all strains were omitted. The epidemic curve based on the number of isolates collected during the study period showed two different picks of outbreak separated by 46 days in November 2012 and January 2013. The Bayesian tree indicated that *K. pneumoniae* strains isolated during the study period could have been introduced in the hospital setting since the end of the year 2007. Moreover, the phylogenetic tree showed two different epidemic entrances in the years 2008 and 2009. Bayesian molecular epidemiology resulted a powerful tool to improve multi-drug resistant pathogen surveillance and develop effective interventions to prevent nosocomial outbreaks or constant strains reintroduction.

RECURRENT HERPES SIMPLEX VIRUS 1 (HSV-1) INFECTIONS AND ALZHEIMER'S DISEASE: A POSSIBLE ROLE FOR OXIDATIVE STRESS

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Several evidence suggest HSV-1 as a potential risk factors for Alzheimer Disease (AD), a neurodegenerative disorder characterized by the accumulation in the brain of β-amyloid peptides (Aβs) and neurofibrillary tangles, mainly composed by hyperphosphorylated tau. Despite the numerous data showing specific neurotoxic effects in neurons, the mechanisms underlying HSV-1 related neural damages have to be still defined in detail. Herein we designed *in vivo* study to demonstrate the causal relationship between the multiple viral reactivations in the brain and the appearance of molecular and functional hallmarks of AD. Moreover, since oxidative stress plays a key role in neurodegenerative and neuroinflammatory processes, we analysed oxidative stress hallmarks in cultured neurons and in our *in vivo* model of recurrent HSV-1 infections.

Methods. BALB/c mice were inoculated via snout abrasion with HSV-1, virus reactivation was periodically induced by thermal stress, and virus replication in the brain was verified through PCR and RT-PCR analysis of viral TK gene and ICP4 mRNA. AD-like hallmarks were analyzed in brain tissues by western blotting (wb) and Immunofluorescence (IF). Oxidative stress marker levels, i.e. Reactive Oxygen Species (ROS), 4-hydroxynonenal (HNE, marker of lipid peroxidation), 3-nitrotyrosine (3NT, marker of protein nytrosylation) and carbonylated proteins, were measured both in HSV-1-infected neuronal cells and in brains of mice undergone recurrent HSV-1 infection by fluorimetry and wb. Redox proteomic was used to identify those HNE-modified proteins mostly modulated by recurrent HSV-1 reactivations into the brain.

Results. We found that HSV-1 infection *in vitro* induces in neurons a significant increase in ROS and HNE levels 4 hours after virus infection. Following HSV-1 multiple reactivations, we found in mouse brains: 1) viral TK and ICP4 genes in cortex and hippocampal tissues, indicating that HSV-1 is able to reach and replicate in those brain regions mostly affected during AD; 2) accumulation of Aβs and altered tau phosphorylation; 3) signs of neuroinflammation. 4) high levels of HNE, 3NT, carbonylated proteins, and some HNE-modified proteins modulated by the virus.

Discussion and Conclusions. Overall, our data support the hypothesis that repeated HSV-1 infections may contribute to the neurodegeneration typical of AD and suggest the involvement of virus-induced oxidative stress in this process.

MONITORING *AEDES ALBOPICTUS* AND THE RISK OF ARBOVIRUS TRANSMISSION IN ROME, ITALY

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The colonization of Europe by *Aedes albopictus* (Asian tiger mosquito) in the last decades has created significant nuisance problems as well as autochthonous cases of Chikungunya (CHIKV) and Dengue (DENV) transmission. Nowadays the introduction of infected travellers returning from endemic countries and the presence of this well-adapted and competent vector represent a public health risk for Mediterranean countries. Mathematical and statistical models have been developed to estimate the risk of arbovirus transmission in non-endemic European countries, but predictive accuracy and reliability are yet difficult to achieve due to several constrains, i.e.: i) most of current understanding of arbovirus transmission dynamics relying on data from endemic countries; ii) likelihood of introduction of an infected host or vector often neglected or unknown; iii) lack of adequate mosquito abundance estimates.

We developed a probabilistic model considering both the risk of introduction and the transmission processes for three viruses (CHIK, DENV, ZIKA) in Rome. Data and estimates of parameters values were obtained from previous work regarding the Italian mosquito population and overnight stays of travellers at Rome. Different prevalence of CHIK, DENV, ZIKA in endemic countries resulting in different introduction probabilities and different local vector to host contact ratio were considered in competing scenarios. Frequency of introduction was lower than estimated by flight passenger data, but consistent with number of infected travellers reported by the Nation Health System for the Lazio region. Risk of transmission was high for the CHIK and DENV when vector to host contact ratio (eg: the number of bites per person) was in the range of that observed in highly infested area of Rome, but the probability of outbreak was negligible when averaged on the whole metropolitan area.

This highlights the importance of understanding how the patchy mosquito distribution intersects with the dispersal of incoming infected host. Therefore, the correct estimate of adult female mosquito abundance is essential to assess the risk of arbovirus transmission and appropriately plan preventive measures and control interventions. We tried to estimate this parameter based on available data from retrieved routine *Ae. albopictus* monitoring activities by ovitrap (a small device that collects mosquito eggs) and showed that the number of eggs in ovitraps only approximately correlates with host-seeking adult *Ae. albopictus* abundance. This warns about the reliability of monitoring schemes based exclusively on ovitrap collections to estimate numbers of biting females and plan control interventions.

ANALYTICAL EVALUATION OF QUANTIFERON-PLUS AND QUANTIFERON- GOLD IN-TUBE ASSAYS IN SUBJECTS WITH OR WITHOUT TUBERCULOSIS

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Interferon-γ release assays are diagnostic tests to identify subjects with Latent Tuberculosis Infection (LTBI). The QuantiFERON-TB Gold Plus (QFT-Plus) represents the new generation of the QuantiFERON-TB Gold In-tube (QFT-GIT), the main differences is the addition of a new test tube containing shorter peptides stimulating CD8 T-cells. Aim of this study is to evaluate the accuracy of the QFT-Plus compared with the QFT-GIT in a cross sectional study of healthy controls and individuals prospectively enrolled as active TB, cured TB or LTBI.

We enrolled 179 participants: 19 healthy donors, 58 LTBI subjects, 33 cured TB and 69 active TB patients. QFT-Plus and QFT-GIT assays were performed. The response to QFT-Plus was evaluated as single or combined response to TB1 and TB2.

The two tests showed a substantial agreement and similar sensitivity in active TB, and same specificity in healthy donors. A higher proportion of the LTBI subjects responded concomitantly to both TB1 and TB2 compared to those with active TB (97% vs 81%). Moreover, if a selective response to TB2 was observed, this associated with active TB (9%) and with a severe grading of the disease, indirectly demonstrating that TB2 stimulation induces a CD8 T-cell response in absence of a CD4-response.

In conclusion, QFT-Plus and QFT-GIT assays showed a substantial agreement and similar accuracy for active TB detection. Interestingly, a higher proportion of the LTBI subjects responded concomitantly to both QFT-Plus antigens TB1 and TB2 compared to those with active TB, whereas a selective TB2 response associated with active TB.

GENOMIC AND FUNCTIONAL STUDY OF *AEDES ALBOPICTUS* IN ITALY

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During the las decades the Asian tiger mosquito, *Aedes (Stegomyia) albopictus*, vector of numerous arboviruses, including Dengue and Chikungunya, has become a global health concern, spreading from its native range in Southeast-Asia all across the world. In Europe *Ae. albopictus* has been reported for the first time in 1979 in Albania and in 1990 in Italy where it vectored a Chikungunya outbreak in 2007. Until now few studies have been performed to understand the population structure in Italy and to gather the information necessary to develop efficient vector control programs.

We took advantage of an extensive network of collaborators to collect 9 *Ae. albopictus* populations across Italy and 2 additional populations from Albania and Greece in order to:

1- assess levels of susceptibility to pyrethroid insecticides commonly used to reduce the mosquito abundance in Italian urban areas (permethrin, cypermethrin and deltamethrin). Results of bioassays performed according to WHO guidelines showed that most *Ae. albopictus* populations are highly susceptible to all the tested pyrethroids. Only populations from Emilia Romagna and Greece showed reduced sensibility to permethrin, with mortality rates below the 90% threshold defined by WHO as indicative of confirmed resistance and the 98% threshold indicative of suspected resistance, respectively. These represent the first reports of insecticide resistance in *Ae. albopictus* in Europe raising alarm of its possible spreading and increase in future years. 2- reconstruct possible sources of invasion of Italy, as well as the subsequent population structuring. In collaboration with Department of Ecology & Evolutionary Biology in Yale University, we genotyped by ddRAD sequencing approximately 90,000 SNPs in 77 individuals.

Population genomic structure analysis, carried out including a reference SNPs dataset from 20 previously genotyped worldwide native and invasive populations, revealed: i) different source populations for Italy and Albania (Japanes/American populations) compared to Greece (Southeast-Asia populations); ii) invasion of Italy by at least two different source populations and possible processes of admixture among different invasive populations creating a complex genomic pattern; iii) high genetic diversity within Italy suggesting multiple invasion events and/or high propagule pressures; iv) low inter-population genetic differentiation with slight signs of isolation by distance.

Further studies are needed to better understand the ongoing invasion process and to evaluate if differences in source populations could correlate with differences in susceptibility to insecticides.

COLONIZATION OF HUMAN GUT BY GENOTOXIC MUCOSA-ASSOCIATED *ESCHERICHIA COLI* AND COLORECTAL CANCER RISK: FOCUSING ON GENOTYPING AND VIRULENCE

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Introduction. Some B2 phylogenetic group of *Escherichia coli* (*E.coli*) harbor a (*pk*s) pathogenicity island that encodes the multi-enzymatic machinery for the synthesis of a genotoxin called colibactin. The ability *of pks+ E. coli* strains to promote tumorigenesis is linked to the property of colibactin to induce double-stranded DNA breaks, cell cycle arrest, and megalocytosis in eukaryotic cells that might contribute to tumor promotion and cancer progression. The aim of this study was to assess if B2 *pks+ E. coli* strains could colonize precancerous lesions, such as colon polypoid lesions, and affect colorectal cancer (CRC) development.

Materials and Methods. In this cross-sectional study, a total of 1,500 *E. coli* isolates collected from twenty polyp biopsies, twenty biopsies of normal tissues adjacent to the lesions and ten healthy control specimens enrolled in this project. *pks* island frequency, phylogenetic grouping, fingerprint genotyping, and virulence gene features of *pks+ E. coli* isolates were performed. *E. coli* strain IHE3034 was used as *pks+* control.

Results. A total of 88 *pks+ E. coli* isolates collected from polyploidy patients were identified and characterized. *pks* island with an high relative abundance of 75.3% and 62% was found in polyp lesions and the normal tissues adjacent to the lesions of two patients, respectively. Distribution of *E. coli* phylogroups among *pks+* isolates showed that predominant phylogroups was B2 (84/88; 95.45%), followed by D (4/88; 4.54%). Clustering based on fragment profiles of composite analysis, typed the isolates into 5 major clusters (I-V) and 17 sub-clusters. The most prevalent virulence genes among *pks+ E. coli* were *fimH* and *fyuA* (100%), *vat* (89%), *hra* (69%), *ibeA* (67%), and *papA* (64%).

Conclusions. Altogether, our results revealed that *pks+ E. coli* can abnormally colonize the precancerous lesions, with a high distribution extended in both the polyp lesions and in normal tissue adjacent to the lesions. The high differences in fingerprinting patterns obtained indicate that the *pks+ E. coli* strains were genetically diverse, possibly allowing them to more easily adapt to environmental variations. However, further studies are necessary in order to assess the *pks+ E. coli* role in the CRC progression.

PROBIOTICS MODULE TH1/TH17 AND IFN RESPONSE IN HIV PATIENTS ON SUPPRESSIVE cART

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The complex relationship among the Th1/Th17 lymphocytes and innate antiviral defences in the intestinal mucosa during HIV-1 infection has not been well characterized. Ten ART treated HIV-infected subjects underwent endoscopic procedures and blood collection prior to initiation of probiotics supplementation (T0) and after 6 months (T6). Mucosa biopsies were obtained from five different intestinal sites; Lamina Propria Lymphocytes (LPLs) were isolated. Cell phenotype (CD3, CD4, CD45Ro, CD27) and activation markers (CD38 and HLA-DR) were detected on freshly samples. Th1 and Th17 cell phenotype were detected by IL-17A and IFNγ intra-citoplasmatic staining, respectively, after overnight PMA and ionomycine activation. IFNα subtypes, IFNβ, IFNR1, IFNγ mRNAs were quantified by RT-PCR. Data were analyzed by Wilcoxon signed-ranked test (paired data) and Spearman's correlation using SPSS v22.

Intestinal and blood Th17 and Th1 frequencies at T6 were increased in CD4 population and in EM (Effector Memory) and CM (Central Memory) subpopulations. A reduction of CD38 and HLA-DR was observed at T6 in CD4 and in all EM and CM subpopulations. The most statistically significant increase in Th17 frequencies in gut was observed in CM population and this level at T6 was inversely correlated to the percentages of CD4 cells expressing HLA-DR in EM subpopulation ($r=-0.79$ $p=0.006$). We were observed the same results in the CD8+ cells for the immune activation: a reduction of CD38 and HLA-DR expression in all different subpopulations. A decrease in IFNγ expression and an increase in IFNα subtypes (10, 14, 17 and 21) expression were recorded at T6 in gut whereas no such differences were observed for the other IFN genes analyzed in gut and peripheral blood compartments.

Probiotics supplementation for 6 months in HIV+ individuals on effective ART induced a marked recovery in the levels of both Th17 and Th1 cells, a significant reduction of cellular markers of activation and specific modulation of IFN-mediated immunity in GALT and in peripheral blood.

AUTHOR'S INDEX

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