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IMPLEMENTATION OF CORONARY ARTERY PHANTOM WITH HYPEREMIA

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Fractional flow reserve (FFR) and coronary flow reserve (CFR) are the indices to diagnose ischemia in coronary artery diseases. To obtain these indices, hyperemia, the increased blood flow through vasodilation, is used as a reference and this occurs when adenosine is injected *in vivo*. However, for phantom models in previous studies, most researchers didn't consider hyperemia condition. This study aims to implement hyperemia in coronary artery phantom. We have constructed a circulation phantom to mimic coronary flow system. A coronary artery pressure consists of forward and backward waves. Hyperemia was simulated by the total occlusion of backward flow when the pressure was decreased, and flow velocity was increased. Doppler test fluid was used as the flow medium. A reservoir was made to implement the venous system. To realize the coronary artery stenosis, area ratios of 40%, 70%, and 88% stenosis model were made. The pressure and the flow velocity inside the tube were measured with a catheter (ComboWire XT, Philips Volcano, USA). When the mean pressure of the vein was 10 mmHg, FFR values were 0.93, 0.74, and 0.53 with back flow, and 0.80, 0.63, and 0.42 in hyperemia state, CFR values were 2.2, 1.5 and 1.2 at the stenosis rates of 40%, 70%, and 88%, respectively. When the mean pressure of the vein was increased to 30 mmHg, FFR values were 0.99, 0.95, and 0.69 with back flow, and 0.89, 0.85, and 0.59 in hyperemia state, CFR values were 2.5, 1.6 and 1.2 at the stenosis rates of 40%, 70%, and 88%, respectively. We successfully implemented an *in vitro* coronary artery system that can measure FFR and CFR values according to pressure of the vein and the degree of stenosis. It is expected that phantom model helps to understand the physiology of a coronary artery diseases.

BIOGRAPHY

Soohong Min is pursuing his doctorate from Jeju National University in Korea. He is interested in the diagnosis and treatment of cardiovascular disease. More specifically, he is interested in morphological and hemodynamic information in blood vessels. He is also interested in medical ultrasonic field.

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GENETIC VARIABILITY OF PEPTIDYL ARGININE DEIMINASE FROM *PORPHYROMONAS GINGIVALIS* IN PERIODONTITIS PATIENTS

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Introduction & Objective: Periodontitis is a widespread chronic inflammatory disease. Untreated condition leads to progressive destruction of the periodontal tissue and may result in tooth loss. Changes in oral microbiome leading to periodontitis are mainly driven by *Porphyromonas gingivalis*, the pathogen producing numerous virulence factors, including peptidylarginine deiminase (PPAD). PPAD modifies C-terminal arginine to citrulline, causing changes in structure and function of modified proteins, contributing to development periodontitis. The aim of this study was to investigate variability of PPAD in clinical isolates of *P. gingivalis*.

Materials & Methods: Together 23 *P. gingivalis* strains were isolated from patients with periodontitis and the PPAD gene was sequenced and analyzed together with sequences extracted from the GenBank database. Identified differences in the sequence were introduced into PPAD in reference strain ATCC 33277 and expression (mRNA) and PPAD activity were measured in cultures of the mutant. PPAD variants were expressed in *P. gingivalis*, purified and used to compare their enzymatic properties. Clinical parameters of periodontitis severity in patients infected with different *P. gingivalis* strains were determined.

Results: A new form of PPAD with three amino acid substitutions (G231N, E232T, N235D) near the active site was found in approximately 30% of *P. gingivalis* strains. Introduction of those mutations into the PPAD sequence in the ATCC 33277 strain resulted in two-fold increase of PPAD activity in culture, without effect on the level of mRNA expression. Kinetic assessment of the enzymatic reaction revealed that the mutated form of PPAD had higher maximum reaction rate (V_{max}). Patients infected with *P. gingivalis* strains with the super active PPAD variant had more advanced damage of periodontal tissues.

Conclusion: The newly identified form of PPAD shows higher enzymatic activity and its presence in strains of *P. gingivalis* in periodontitis patients correlated with severity of the disease.

BIOGRAPHY

Grzegorz Bereta has completed his MSc in Molecular Biotechnology at Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University, Krakow, Poland and since then he is enrolled on PhD studies at the same faculty. He has authored two publications and two conference reports as well as one book chapter.

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CAPSULAR HEPTOSE SYNTHESIS PATHWAY OF *CAMPYLOBACTER JEJUNI* AS A NEW TARGET TO PREVENT CAMPYLOBACTERIOSIS

Carole Creuzenet
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Campylobacter jejuni (CJ) is a commensal in poultry but is also a human bacterial pathogen. It is a predominant cause of bacterial enteritis worldwide and, in developed countries, campylobacteriosis is associated with consumption of undercooked poultry meat that had been contaminated by CJ during slaughter. CJ's capsule is an external polysaccharide important for colonization and virulence that comprises a modified heptose in most strains. We investigate the biological roles and the biosynthetic pathways of these heptoses with a view to inhibit their synthesis in poultry before slaughter, which would decrease the CJ load in poultry meat and prevent harmful transmission to humans. We deciphered the activity of seven enzymes involved in modified heptoses synthesis in two CJ strains, revealing unexpected functions and specificities of novel C3/C5 epimerases and C4 reductases that could be targeted for inhibition. Knockout mutagenesis studies of heptose modifying genes in strain NCTC 11168 showed that heptose modification is not necessary for capsule synthesis but affects bacterial resistance to serum and bile salts, biofilm formation, adhesion to intestinal epithelial cells and their invasion. The mutants also showed slightly decreased phagocytosis by macrophages. Most importantly, we also demonstrate that heptose modifying genes are important for colonization and persistence of *C. jejuni* in chicken. These findings suggest that fine tuning the capsule composition via heptose modification contributes to host pathogen interactions and likely host specificity. This work also provides new enzyme targets to screen for inhibitors that could be used to decrease campylobacteriosis by application to chickens pre-slaughter. It also provides new tools to synthesize carbohydrate antigens useful for chicken vaccination and provides grounds for the elucidation of similar pathways of other pathogens.

BIOGRAPHY

Carole Creuzenet has completed her PhD in Biochemistry at the University of Nantes and the National Institute for Agronomical Research (France) and her postdoctoral studies at the Massachusetts Institute of Technology (USA) and the University of Guelph (Canada). She is Associate Professor at the University of Western Ontario (London, Canada) where her lab focuses on virulence factors from bacterial gastrointestinal pathogens such as *Campylobacter jejuni, Helicobacter pylori and Yersinia pseudotuberculosis*. Her focus is on glycolipids and glycoproteins as well as on novel secreted proteins and their folding partners. She has published 38 papers in reputed journals with h-index of 19.

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HEAVY METAL AND ANTIBIOTIC RESISTANT BACTERIA ISOLATED FROM GUHESWORI SEWAGE TREATMENT PLANT, NEPAL

Bikram Gautam[1,2] and **Rameshwar Adhikari**[2]
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The aim of this project is to simply determine the resistance level of microorganisms isolated from the treated sewage effluent. To accomplish this first their resistance pattern against antibiotics and heavy metals were screened as per Clinical and Laboratory Standards Institute, 2017 and British pharmacopeia, 2016 respectively. This study also provides evidence that these microorganisms have metabolized the heavy metals and hence might be very useful in tackling problems of metal poisoning due to both spillage and/or due to geographical location. Sewage contains chemicals (biocides, detergents, heavy metals etc.) and microorganisms. Bacteria get exposed to the chemicals and acquire resistance to antibiotic(s) and heavy metal(s). The aim of this study was to the isolated bacteria from the treated sewage and assess resistance pattern of the isolates against antibiotics and heavy metals. Grab sampling was performed from the treated effluent at the Guheswori sewage treatment plant. To assess the resistance pattern for antibiotic(s) and heavy metal(s), antibiotic susceptibility test and minimum inhibitory concentration by cup well method were performed as per Clinical and Laboratory Standards Institute, 2017 and British pharmacopeia, 2016 respectively. *Staphylococcus aureus, Enterococcus faecalis, Citrobacter freundii, Escherichia coli, Enterobacter aerogenes, Proteus mirabilis, P. vulgaris, Salmonella Typhi, Pseudomonas aeruginosa* were isolated from the treated sewage. Multi drug resistant and heavy metal resistant isolates were screened. P. aeruginosa was able to resist the heavy metal concentration up to 10000 g/L dilution of Fe++. Pearson's chi square test shows that there is a significant association ($p<0.001$) between isolates and antibiotic resistance pattern; isolates and heavy metal resistance pattern at dilution 10000 g/L, 5000 g/L, 2500 g/L, 1250 g/L. The findings of the study show that the sewage treatment plant is not capable of effluent polishing. The isolates from treated sewage were found to be resistant to multiple heavy metals and antibiotics. Heavy metal resistant bacteria could be utilized in lower metal pollution through bio-absorption, mineralization, enzymatic oxidation/reduction to a less toxic form etc.

Note:

BIOGRAPHY

Bikram Gautam is a fourth semester MSc Microbiology student at Department of Microbiology, St. Xavier's College, Maitighar, Nepal. He has published three research papers to date. He is serving as a Research Assistant at RECAST and working as a Quality Controller at Senior Shree Krishna Beverage, Kathmandu, Nepal.

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THE CHALLENGES IN MANAGING HEART FAILURE WITH PRESERVED EJECTION FRACTION (HFPEF)

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The learning objectives of the current study is to demonstrate the association between heart failure with preserved ejection fraction (HFpEF) and survival, given a patient with heart failure (HF), recognize HFpEF based on clinical signs and symptoms, physical examination, echocardiography, and radiographic findings, classify patients at high risk of hospitalization and mortality through assessing risk factors, clinical presentation, and interpretation of biomarkers, distinguish the clinical presentation, diagnosis, and treatment strategies of HFpEF from those of HF with reduced ejection fraction, given a patient with HFpEF, develop an individualized treatment plan based on current evidence and assess the potential role of future pharmacotherapies for HFpEF. Approximately half of all patients with heart failure have preserved ejection fraction (HFpEF) and, as life expectancies continue to increase in western societies, the prevalence of HFpEF will continue to grow. In contrast to heart failure with reduced ejection fraction (HFrEF), no treatment has been proven in pivotal clinical trials to be effective for HFpEF, largely because of the pathophysiological heterogeneity that exists within the broad spectrum of HFpEF. This syndrome was historically considered to be caused exclusively by left ventricular diastolic dysfunction, but research has identified several other contributory factors, including limitations in left ventricular systolic reserve, systemic and pulmonary vascular function, nitric oxide bioavailability, chronotropic reserve, right heart function, autonomic tone, left atrial function and peripheral impairments. Multiple individual mechanisms frequently coexist within the same patient to cause symptomatic heart failure, but between patients with HFpEF the extent to which each component is operative can differ widely, confounding treatment approaches. This lecture focuses on our current understanding of the pathophysiological mechanisms underlying HFpEF, and how they might be mechanistically related to typical risk factors for HFpEF, including ageing, obesity and hypertension.

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FLAGELLAR ASSEMBLY IN *SALMONELLA FLHA* DELETED STRAIN AND ITS ROLE IN BIOFILM FORMATION

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Biofilms formation is a major hazardous problem from both clinical and environmental perspective. Flagellum-mediated motility is important for biofilm formation by several gram-negative bacteria. More than 50 genes are involved in flagellar biosynthesis and function in *Salmonella typhimurium*. The flagella basal body is a representative of type III protein secretion systems; used by several gram-negative bacterial pathogens to colonize foreign tissues and substrates. The mechanism of flagellar assembly was analyzed in *S.typhimurium*, using bioinformatics analysis to identify conserved structural elements. In this study, FliI a flagellar protein that is needed for flagellar assembly and may be involved in a specialized protein export pathway was cloned and overexpressed. *FlhA* deleted mutant *Salmonella* strain SJW1616 was used to transform *FliI* overproducing plasmid by electroporation. Using vital dyes (Alexaflour 488), visualization of motility was observed in wild type, SJW1616 (Δ*flhA*) and *FlhA* transductant strain which was further assessed by biofilm formation ability. Swimming, swarming motility along with significantly reduced biofilm formation was observed in SJW1616 (Δ*flhA*) compared to wild type and *FlhA* transductant strains. This study will extend initial evidence that *FliI* plays important role in flagellar export system and flagellum-mediated rotation is critical for swimming, swarming motility and biofilm formation. The flagellar basal body is a particularly convenient drug target, since the architecture of most its components has been determined near atomic resolution and it is an ancient evolutionarily conserved macromolecular assembly. The knowledge gained will also have implications for elucidation of the mechanistic design principles underlying protein secretion complexes.

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HIGH-THROUGHPUT CARBON SUBSTRATE PROFILING OF *MYCOBACTERIUM ULCERANS* SUGGESTS POTENTIAL ENVIRONMENTAL

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Background: *Mycobacterium ulcerans* is a close derivative of *Mycobacterium marinum* and the agent of buruli ulcer in some tropical countries. Epidemiological and environmental studies pointed towards stagnant water ecosystems as potential sources of *M. ulcerans*, yet the ultimate reservoirs remain elusive. We hypothesized that carbon substrate determination may help elucidating the spectrum of potential reservoirs.

Methodology & Results: In a first step, high-throughput phenotype microarray BIOLOG was used to profile carbon substrates in one *M. marinum* and five *M. ulcerans* strains. A total of 131/190 (69%) carbon substrates were metabolized by at least one *M. ulcerans* strain, including 28/190 (15%) carbon substrates metabolized by all five *M. ulcerans* strains of which 21 substrates were also metabolized by *M. marinum*. In a second step, 131 carbon substrates were investigated, through a bibliographical search, for their known environmental sources including plants, fruits and vegetables, bacteria, algae, fungi, nematodes, mollusks, mammals, insects and the inanimate environment. This analysis yielded significant association of *M. ulcerans* with bacteria (p=0.000), fungi (p=0.001), algae (p=0.003) and mollusks (p=0.007). In a third step, the Medline database was cross-searched for bacteria, fungi, mollusks and algae as potential sources of carbon substrates metabolized by all tested *M. ulcerans*; it indicated that 57% of *M. ulcerans* substrates were associated with bacteria, 18% with alga, 11% with mollusks and 7% with fungi.

Conclusions: This first report of high-throughput carbon substrate utilization by *M. ulcerans* would help designing media to isolate and grow this pathogen. Furthermore, the presented data suggest that potential *M. ulcerans* environmental reservoirs might be related to micro-habitats where bacteria, fungi, algae and mollusks are abundant. This should be followed by targeted investigations in buruli ulcer endemic regions.

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PERSONALIZED AND TRANSLATIONAL MEDICINE AS A MODEL OF THE HEALTHCARE SERVICES AND ARMA-MENTARIUM TO GET THE MODEL ARMED: MYTH OR THE REALITY?

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A new systems approach to diseased states and wellness result in a new branch in the healthcare services, namely, personalized medicine (PM). To achieve the implementa-tion of PM concept into the daily practice including clinical cardiology, it is necessary to create a fundamentally new strategy based upon the subclinical recognition of bioindicators (bio predictors and biomarkers) of hidden abnormalities long before the disease clinically manifests itself. Each decision-maker values the impact of their decision to use PM on their own budget and well-being, which may not necessarily be optimal for society. It would be extremely useful to integrate data harvesting from different databanks for applications such as prediction and personalization of further treatment to thus provide more tailored measures for the patients and persons-at-risk resulting in improved outcomes whilst securing the healthy state and wellness, reduced adverse events, and more cost-effective use of health care resources. One of the most advanced areas in cardiology is atherosclerosis, cardiovascular and coronary disorders as well as in myocarditis. A lack of medical guidelines has been identified by most responders as the predominant barrier for adoption, indicating a need for the development of best practices and guidelines to support the implementation of PM into the daily practice of cardiologists! implementation of PM requires a lot before the current model physician-patient could be gradually displaced by a new model medical advisor-healthy person-at-risk. This is the reason for developing global scientific, clinical, social and educational projects in PM to elicit the content of the new branch.

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LACTOBACILLUS CASEI COULD BE A BIO-THERAPEUTIC FOR ENTERIC BACTERIAL INFECTIONS

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As a major source of microbes and their numerous beneficial effects, the gut microflora/microbiome is intimately linked to human health, immunity and diseases. The key intestinal microbial byproducts, commonly known as metabolites, are crucial to the maintenance of a balanced gut ecosystem and healthy gut microbial community. More specifically, the presence or absence of several genes and their expression levels, in the presence or absence of stimuli or stress, regulate the production and concentration/number of various metabolites. These are essential for host defense and immunity and protecting from various diseases or pre-condition of diseases including inflammation, cancer, oxidation, atherosclerosis, and out competition of enteric bacterial pathogens. In a recent study, we found that in the presence of the prebiotic-like component peanut flour, *Lactobacillus casei* (LC) produced 100 times more linoleic acid (LA) than under normal conditions and was able to outcompete several enteric bacterial pathogens. Based on this evidence, we have overexpressed the linoleate isomerase (myosin cross-reactive antigen, *mcra*) gene in a natural, sustainable, bacteriophage-resistant LC strain (LC^{+mcra}) to enhance the production of conjugated linoleic acids (CLA) and verify the ability of this genetically engineered strain LC+mcra to inhibit growth, colonization, and infection of host cells by human enteric foodborne bacterial pathogens. We found that LC^{+mcra} excluded the Salmonella and EHEC in co-culture condition and altered the host cell-pathogens (both) interactions. The genetically modified mutant also altered the virulence properties of both bacterial pathogens significantly. This study showed that LC^{+mcra} could be a non-traditional bio-therapeutic for preventing the colonization of *Salmonella* and EHEC.

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ELECTRON MICROSCOPIC STUDIES OF BRAIN TISSUE IN FETUSES FROM SCHIZOPHRENIC MOTHERS

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The neurodevelopmental theory in the aetiology of schizophrenia is considered one of the most consistent at present. Evidence from epidemiological and neuropathological studies indicates that the pathogenic process that culminate in the development of schizophrenia are initiated early in life and has been associated with a variety of prenatal environmental insults to the developing brain, including infection. Although the infectious agents have been proposed as one of the risk factors for schizophrenia the data on the association of a specific infectious agent with prenatal brain evidence is absent. Understanding of the structural abnormalities would allow a better identification of neurodevelopmental processes that contribute to risk for schizophrenia. We have hypothesized that at ultra high-risk fetuses would have alterations at cellular level that would let us differentiate them to the comparison subjects. A reappraisal of our ultrastructural studies carried out in samples of the left temporal lobe of fetuses at ultra-high risk of developing schizophrenia is presented. The findings obtained are compatible with an active infection of the central nervous system by herpes simplex hominis type I [HSV1] virus. The present results are the first direct evidence that demonstrate the presence of this virus in the central nervous system of fetuses from schizophrenic mothers in the critical period of fetal development. The importance of this finding can have practical applications in the prevention of the illness keeping in mind its direct relation to the aetiology and physiopathology of schizophrenia.

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WORLDWIDE SPREAD OF MDR BACTERIA SIGNALS TO BE RESIDENT OF GUT MICROBIOTA FOR VITAMIN SYNTHESIS AND HETEROGENEOUS PHYTO-ANTIBIOTICS MAY CURE MDR INFECTIONS GLOBALLY

Asit Kumar Chakraborty
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WHO advocates worldwide action plan promoting research on phyto-antibiotics, gene medicines and conventional anti-microbials to stop superbugs horror that claims million deaths due to ineffectiveness of antibiotics. WHO has also recommended controlled use of antibiotics in patients and bans use of excess antibiotics in agricultural land and food animal growth. Our study indicated that more than 40% of sea, river and rain water bacteria were resistant to semi-synthetic antibiotics like ampicillin and amoxicillin. *blaTEM, blaCTX-M, blaOXA* types beta-lactamases, *AacC1/A1* acetyl transferases and AphA4 phospho transferases including *catB3, sul1/2 and strA/B* genes were detected in most plasmids and certain MDR chromosome islands as in *E. coli, P. aeruginosa, K. pneumoniae, S. enterica, M. tuberculosis, S. aureus and A. baumannii*. Plasmids carrying blaNDM1 and blaKPC genes are increasing and wonder drug imipenem is becoming useless in few cases and Mcr-1 gene in E. coli plasmids has made colistin drug useless. *TetA/C, acrAB-TolC, mexAB/CD/EF-oprM, macAB, mtrCDE* drug efflux genes were activated causing many antibiotics (tetracycline, azithromycin, amikacin, norfloxacin) useless. *RpoB, pncA, ponA, penA, and rpsL* mutations are involved in multi-resistance in TB and gonorrhoea. *GyrA/B or parC* genes mutations and *aac6'-1b-cr* gene accumulation were the cause of widespread fluoroquinolones (ciprofloxacin) drug resistance mtrR, acrR, tetR and ampR types transcriptional regulators have also accumulated in superbug plasmids and are activated by antibiotics increasing superbug sepsis and death. PubMed and GenBank search indicated antimicrobial resistance (AMR) had created an acute problem in modern society worldwide and could be designated as 21st century pseudo antibiotic dark age. Abundant multi-drug resistant (MDR) bacteria from Kolkata Ganga River and Digha Sea were detected and characterized as Extended Spectrum Beta-Lactamases (ESBL) superbugs (*Escherichia, Phenalkaligenes, Pseudomonas, Streptococci, Citrobacter, and Stenotrophomonas*). AMR could be resembled to many hallmarks of cancer cells: MDR genes in plasmids similar to diversified oncogenes, active mutations producing ESBL and inhibitor resistant similar to GTP-bound Gly->Val mutant Ha-ras oncoprotein, activation of *blaCTX-M, acrAB, tetA and cmr* genes with high copy number and expression, similar to over expressed retroviral oncogenes and high amount of small plasmid-like DNAs apart from large conjugative plasmids similar to high copies of chromosomes and miRNA in tumour cells. However, we have forgotten that 2x1012 bacteria in the intestine are constantly synthesizing 20 vitamins and complex bio-molecules for our body and one high dose of antibiotics is enough to kill all such microbiota. Thus, it appears, multidrug-resistant genes creation is to protect microbiota from repeated doses of antibiotics that we have consumed since 1940s. Thus, MDR bacteria will be the resident of intestine favouring vitamin biosynthesis, needed for normal human metabolism. Several high-quality research from US Human Microbiome Project (HMP), European Metagenomics of the Human Intestinal Tract (MetaHIT) and others have demonstrated the beneficial functions of the normal gut flora (>35000 species) on health. It is thus G-20 nations in Germany are united for active research on MDR bacteria to stop superbug horror. Interestingly an improved MDR-cure organic phyto-extracts (*Cassia fistula, Suregada multiflora, Syzygium aromaticum and Cinnamomum zeynalicum etc*) inhibits Kolkata superbugs and gives a hope for new drug development as we have characterized active chemicals by MASS, NMR and FT-IR.

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QUALITY OF MEDICAL CARE DELIVERED TO THE PATIENTS IN GOVERNMENT HOSPITALS IN THE CITY OF KARACHI

Hira Sabir Malik
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The first major objective of this study is to explore the service quality level of Public Hospitals in the city of Karachi from perspective of patients. Secondly, the satisfactions level of the ailing patients towards the services provided by these health care government sectors in general is investigated. The measurement instrument used in this study is based on questionnaires. Customer satisfaction and service quality are often treated together as functions of customer's perceptions and expectations. Research has shown that high service quality contributes significantly to customer satisfaction and customer delight. This study empirically explores the relationship between hospital quality management and service quality performance for a sample of patients of government health care hospitals in the city of Karachi. SERVQUAL model has been adopted to encompass various aspects of service quality. The study has been undertaken to demonstrate the Gaps for measuring patient's perceptions-expectation of health care services quality in government hospitals in the city of Karachi. In this study an attempt has been made to explore the service quality gap which is called gap score by means of making a comparison between customers' expectations and their actual perceptions towards the services and the government hospital patients are treated in. The purpose of this research is to provide review of the SERVQUAL research in measurement of health care service quality, to obtain information about quality parameters of services provided by govt hospitals of Karachi and to find out as to how much these parameters rate is as per the expectations of the patients. A sample size of 150 ailing patients is taken from department to department in different government hospitals situated in the city of Karachi. The results have shown an alarming situation where government hospitals are far away from the patient's expectations. Furthermore, there is an extreme need for training in public hospital staff and their attitudes towards the ailing. Looking at the situation it is highly recommended that the government should take a country wide initiative to launch special programs where hospitals internal structures and work process are re-organized on the principles of quality management practices, through the introduction of ISO Programs. This would help in improving the service quality at each stage of the services provided by these hospitals.

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THE EFFECT OF POMEGRANATE EXTRACT ON SURVIVAL AND PERITONEAL BACTERIAL LOAD IN CECAL LIGATION AND PERFORATION MODEL OF SEPSIS RAT

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Sepsis is one of the major causes of death in intensive care units. Oxidative stress and hyper-inflammation has been shown to be major cause of mortality and morbidity in septic cases. Pomegranate is a fruit which is considered for its antioxidant and anti-inflammatory properties. The aim of this study was to evaluate the effect of POMx, a standard pomegranate extract, on mortality and peritoneal bacterial load in cecal ligation and perforation (CLP) model of sepsis in rats. Male Wistar rats were divided into four groups: sham; CLP; prevention [consumed POMx (250 mg of polyphenols/kg/day) for four weeks and subjected to CLP]; treatment [subjected to CLP and then received a single drink of POMx (250 mg of polyphenols/kg)]. Sepsis was induced by CLP surgery. 10 days survival rate of all groups (subdivided into with and without antibiotics subgroups) were recorded. Peritoneal bacterial load of animal was also assessed. Data were analysed using log-rank and Kruskal-Wallis tests. There were no significant differences in survival rates of CLP, prevention and treatment groups, in subgroups without antibiotics. However, in subgroups with antibiotics, the prevention group had significantly lower survival rate than sham group ($p<0.05$). Conversely, the bacterial load of prevention and treatment group were significantly higher than sham group ($p<0.01$). In conclusion, our study demonstrated that pomegranate extract could increase mortality rate via increasing peritoneal cavity bacterial load, in CLP model of sepsis. More studies to assess mechanisms of this effect are warranted.

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EPIDEMIC FLU VIRUS

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For the emergency created by the epidemic of influence of the pigs in Mexico it was correct not to create alarmism's being victims of a bad information. The possibility that the virus arrives in other parts of the world is real as for all the types of influence virus. In order that a strain has a wide distribution, its antigenic characteristics must ensure that it escapes the neutralization of antibodies of the host and of the surrounding population. So, the outbreaks will happen with those strains that have dominant antigens that fit the deficiency, or better, the absences of antibody in the population. It seems, in conclusion that the flu virus shows an ability and an aptitude for survival built on the possibility of emergence of new models that allow the virus being confused easily through populations still partly immune to previous antigenic forms. According to this view, the changes in the influenza A can be designed in single meaning, in the context of a principle and of an evolutionary progress, from Burnet said immunological drift or steering immunology. The antiviral drugs (inhibitors of the neuraminidases, receptor of the virus surface) should be assumed within 48 hours by the appearance of the influence symptoms and for the subjects that have had a close contact with people infected by the flu virus. The vaccination against the influence is the most effective method to prevent the illness. From the moment that we find the isolation of a new flu virus, we must wait for the preparation of a new specific vaccine that will be ready for the next influence season in Autumn.

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THREAT FOR PANDEMIC EMERGENCE OF NEGLECTED CARDIOVASCULAR DISEASE

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Forgotten diseases of poverty and tropical infections as classified by Center for Disease Control (CDC) affect millions of people in United States alone. As an example, Chagas' disease is a vector and food-borne as well as sexually transmissible disease which threatens a global epidemic if not eradicated soon. Over 300,000 patients are diagnosed in USA, and six-eight million patients suffer from Chagas' disease in Latin America. Centre for Tropical and Infectious Diseases in Negrar (Verona), in Florence, Italy reported that 4.2% of patients are serologic positive for Chagas' disease. It is estimated that 4.2% of Latin-Americans in Europe to be affected by Chagas' disease and a major portion resides in Italy. Contaminated fruit juice and surge of immigrants, blood and organ transplants are responsible for the global spread of the disease. In acute stage patients develop fever, cardiovascular complications and myocarditis. In addition, 30-40% patients progress to chronic cardiomyopathy after 10-20 years, as latent organisms in pseudocysts rupture free to attack and damage neurons and ganglia. The organisms harbor sophisticated molecular and signaling structures; yet actively alter the host cardiomyocytes' specific G proteins and Ca channels signaling pathways and modulate prostaglandins and cytokines to render them ineffective and to support invasion. MicroPET and MRI studies in models demonstrate cardiac altered structure and dysfunction during acute myocarditis as well as chronic cardiomyopathy. In this presentation, pathogenesis and epidemiology of opportunistic and infectious diseases will be scrutinized with emphasis on cardiovascular complications and possible epidemic and pandemic outbreak.

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DEVELOPMENT OF AORTIC FISTULAS INTO THE BRONCHIAL TREE AND LUNG PARENCHYMA FOLLOWING CARDIAC SURGERY

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Aortic fistulas into the airways may develop after unpredictable periods after surgery and are often the consequence of pseudoaneurysms. They are more common after descending thoracic aorta (DTA) procedures. Postoperative aortic pseudoaneurysms (PSAs) may arise from disruption of one or more arterial wall layers with extravasation of blood into the surrounding spaces. The hematoma is then held by the remaining vascular layers, fibrous tissue, and sometimes the parietal pericardium. A neointima may develop. Disruption may be related to different sites depending on the type of operation. A PSA is not the only possible cause of bronchopulmonary damage, which may also be due to neoaneurysms involving the native aortic wall next to suture lines. In other cases slow but continuous damage to lung parenchyma is caused by strictly adjacent foreign material such as graft substance, remnant of temporary bypass, silk knots and suture material, endobronchial expandable metal stents, or kinking of an aortic stent-graft. Hemoptysis is the first (and often the only) symptom of aortic fistulas into the bronchial tree or lung parenchyma. It may be massive or intermittent, depending on the size of the opening. If left untreated, ABPFs are uniformly fatal. Management of the airways must be immediate and must first include bleeding control by selective endotracheal intubation. The inflated cuff of a Carlens tube or a Fogarty embolectomy catheter may be positioned into the bleeding side of bronchial tree to protect the contralateral side from hemorrage. Otherwise a single-lumen endotracheal tube may be positioned in the healthy main stem bronchus. Various approaches have been described, either surgical or endovascular. When the fistula is located in the ascending aorta, femoral–femoral cannulation should be established before opening the sternum, as the false aneurysm may potentially rupture during sternotomy.

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HOSPITAL OUTCOME OF ACUTE HYPERGLYCEMIA AND TNF-A IN PATIENTS WITH ST-ELEVATION MYOCARDIAL INFARCTION

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Aims: The aim of the study is to test whether hyperglycemia and inflammation detected in patients with acute ST-elevation myocardial infarction (STEMI) is a predictor of in-hospital major adverse cardiovascular events (MACEs).

Methods: 81 patients with an acute STEMI were enrolled in this clinical study. The studied patients were classified into three groups, group I included patients with a plasma glucose (<200 mg/dl) and no previous history of diabetes, group II included diabetic patients with hyperglycemia and group III included patients with hyperglycemia and no history of diabetes. Tumor necrosis factor alpha (TNF-α), white blood counts (WBCs), and their subtypes were analyzed during hospitalization. The primary end was the composite of mortality, arrhythmia, recurrent nonfatal MI, or heart failure (MACEs) during the hospital stay.

Results: Compared with the other groups, group III patients had significantly higher plasma levels of cardiac biomarkers (troponin I and CK-MB) and inflammatory markers (TNF and WBCs, $p<0.01$) while MACEs developed more among groups II and III groups. 17 (21.8%) patients suffered MACEs mortality in sex patients, heart failure in 13 patients, re-infarction in three patients, atrial fibrillation in three patients and one patient developed heart block. TNFα level, troponin I and the left ventricular ejection fraction were the most independent predictors of the MACEs after acute STEMI. An admission cutoff value of blood glucose level >230 mg/dl cut-off showed sensitivity of 76.5% and specificity of 63.9% as predictor of MACEs.

Conclusion: Hyperglycemia is an important predictor of the outcome in patients hospitalized with acute STEMI. Hyperglycemia is associated with increased levels of inflammatory markers and cardiac biomarkers. TNFα concentrations and hyperglycemia correlated with left ventricular ejection fraction. Inflammatory markers such TNF-α and WBCs counts alone or in combination are strong and independent predictors of outcome in patients with STEMI.

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THE EFFICACY OF *GARCINIA MANGOSTANA* TO REDUCE ENDOTHELIAL DYSFUNCTION AND DYSLIPIDEMIA IN HIGH FRAMINGHAM RISK SCORE PATIENTS

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Background: Endothelial dysfunction and dyslipidemia have an important role in the development of atherosclerotic cardiovascular disease. *Garcinia Mangostana* is an extract of mangosteen that has anti inflamation, immunomodulator, antioxidant, and anti lipid effect. High level of inflamation, lipid profiles, oxidant markers, and circulating endothelial cell (CEC) with low level of endothelial progenitor cell (EPC) predict poor outcomes of endothelial damage. This study was aimed to compare the efficacy of *Garcinia Mangostana* to reduce endothelial dysfunction and dyslipidemia in high framingham risk score to be compare with placebo. Parameters measured are inflamatory markers (IL-6, TNF α, HsCRP), CEC, EPC, and lipid profiles (total cholesterol, HDL, LDL, and triglycerides).

Methods: A randomized, single blind, placebo-controlled clinical trial was conducted in 90 high framingham risk score patients. Study group consumes *Garcinia Mangostana* 5x550 mg for three months as an additional therapy of their regular medications and control group consumed placebo. The data was analyzed by paired t-test for parametric data and wilcoxon test for non parametric data.

Results: Post tests were performed after *Garcinia Mangostana* administration for three months. Inflamation parameters in study group (IL-6, IL-1, and HsCRP) concentration was significantly decreased compared with placebo (−90.85±99.29, 3 pg/ml vs. 50.25±140, 52 pg/ml; P=0.000; −12.08±12, 1 pg/ml vs. 10.3±13.4 pg/ml; P=0.000; and −130.5±106, 3 pg/ml vs. -17.1±71, 7 pg/ml; P=0.000). We also observed significance decrease in total cholesterol, LDL, and HbA1c (−12.52±37.31 mg/dl vs. 1.36±26.25 mg/dl; P=0.05; −18.29±28.6 mg/dl vs. 1.8±18.5 mg/dl; P=0.003; −0.29.±1.1 vs. 0.25±0.78; P=0.012; respectively) when compared to placebo group. There was no difference in HDL, triglycerides and fasting blood glucose. CEC also significantly reduced with increasing of EPC in study group (p=0.000).

Conclusion: The result shows that *Garcinia Mangostana* extract has an efficacy to reduce inflamation (IL-1, IL-6, MDA, and HsCRP), lipid profile, CEC and increase EPC level that reflects an improvement of endothelial function.

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NOVEL COMPOUND HETEROZYGOUS MUTATIONS OF *KCNQ1* IN LONG QT SYNDROME WITH FAMILIAL HISTORY OF UNEXPLAINED SUDDEN DEATH: IDENTIFIED BY ANALYSIS OF WHOLE EXOME SEQUENCING AND PREDISPOSING GENES

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Aim & Objective: This study aimed to identify the pathogenic mutation in a Chinese family with long QT syndrome (LQTs) and unexplained sudden death (USD).

Methods & Results: Whole exome sequencing was conducted for the proband. The genetic data was screened using the 1000 genomes project and SNP database (PubMed), and the identified mutations were assessed for predicted pathogenicity using the SIFT and polyphen-2 algorithms. We identified the compound heterozygous mutations in the *KCNQ1* gene at c. G527A (p. W176X) and c. G1765A (p. G589S) predicted as damaging. The *in-silico* analysis showed that when compared to the characteristics of mRNA and protein of wild-type *KCNQ1*, the mRNA of c. G527A mutation was significantly different in the centroid secondary structure; the subunit coded by W176X would lose the transmembrane domains S3-S6 and helices A-D; the protein secondary structure of G598S was slightly shortened in helix structure; the protein physics-chemical parameters of W176X and G589S significantly and slightly changed, respectively.

Conclusions: The compound heterozygous mutations of W176X and G589S coexisting in *KCNQ1* gene of homologous chromosomes, resulting in more severe phenotype, are the likely pathogenic and genetic risks of LQTs and USD in this Chinese family.