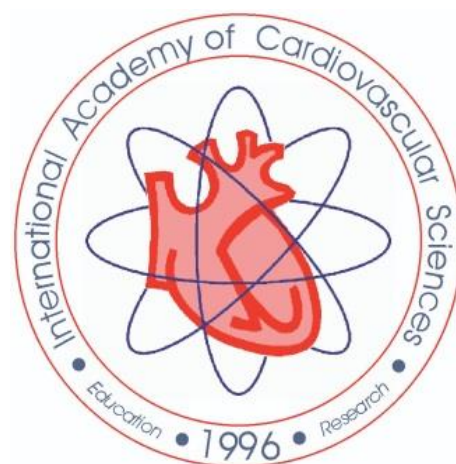


Promoting Cardiovascular Education, Research and Prevention

CV Network

THE OFFICIAL BULLETIN OF THE INTERNATIONAL ACADEMY OF CARDIOVASCULAR SCIENCES

PUBLISHED WITH THE ASSISTANCE OF THE ST. BONIFACE
HOSPITAL ALBRECHTSEN RESEARCH CENTRE



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The International Conference of Cardiovascular Sciences-IACS-India Section Organized by Delhi Pharmaceutical Sciences and Research University, New Delhi, India, February 21-23, 2020

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Delhi Pharmaceutical Sciences and Research University (DPSRU) successfully concluded a three-day International Conference of Cardiovascular Sciences-2020 (ICCS-2020) held during 21-23 February, 2020. The

President, IACS – India Section, Prof. NS Dhalla, Founder, International Academy of Cardiovascular Sciences (IACS), Prof SK Gupta, Emeritus Professor, DPSRU, Prof Raja Babu Panwar, Vice-Chancellor,



Prof. Ramesh K. Goyal, Vice Chancellor, DPSRU delivering welcome address during inauguration ceremony of ICCS-2020

conference was inaugurated by Dr Randeep Guleria, Director, AIIMS in the presence of Prof Ramesh K Goyal, Chairman of the Conference and Vice-Chancellor, DPSRU, Prof Harvinder Popli, Officiating Registrar, DPSRU, Prof CC Kartha, Organizing Secretary and

Rajasthan University of Health Sciences, Jaipur, Prof. Sridhar Dwivedi, Chairman-BOG, DPSRU and Dr Mukesh Nandave, Conference Coordinator and Associate Professor, DPSRU.



Release of Conference Souvenir of ICCS-2020 by Prof. Randeep Guleria, Director, AIIMS, New Delhi and other dignitaries during inauguration ceremony of ICCS-2020



IACS Distinguished Service Award was bestowed upon Prof. Harvinder Popli, Offg. Registrar, DPSRU at the hands of Prof. Randeep Guleria, Prof. N.S. Dhalla and Prof. Sridhar Dwivedi

Special Awards Ceremony:

Prof. C.C. Kartha, President of the IACS- India Section was recognized with the IACS-Lifetime Achievement Award whereas Prof. R.K. Goyal was recognized with the IACS-Distinguished Leadership Award. Prof. R.B.



Dr. Agarwal, President, Heart Care Foundation of India during the mega health camp

Panwar, Vice-Chancellor of Rajasthan University of Health Sciences was honored with IACS-Fellowship. Prof. Harvinder Popli, was recognized with the IACS-Distinguished Service Award in Cardiovascular Sciences. Dr. Mukesh Nandave and Dr. Rajani Mathur were recognized with IACS-India Section Distinguished Services by the SPARCS.

With the theme “connect basic scientists, clinicians including cardiologists and academicians from medical as well as pharmacy colleges”, this majestic international conference witnessed participation of over 600 delegates, 80 speakers from various parts of India and 9 countries. The cardiologists, cardiovascular scientists and young investigators deliberated to solve the problem of heart



IACS Fellowship was bestowed upon Prof. Raja Babu Panwar, Vice Chancellor, Rajasthan University for Health Sciences, Jaipur at the hands of Prof. Randeep Guleria (R), and Prof. N.S. Dhalla (L)

diseases through programs on awareness, prevention, diagnosis, rational treatment and new research. A mega health camp for free screening of lifestyle related disorders was also organised in collaboration with Rotary Club of Delhi Central. The camp was inaugurated by Mr.



Mr. Kuljeet S. Popli, President Rotary Club, New Delhi at the health camp

Sanjeev Khirwar, Principal Secretary, Health & Family Welfare, Delhi Govt.. Mr. Ajay Dutt, MLA, Dr. K.K. Agarwal, President, Heart Care Foundation of India, Mr. Kuljeet Popli, President, Rotary Club of Delhi Central also joined for the inauguration of the mega health camp. Mr. Khirwar, emphasised the need for connecting hospitals, Mohalla Clinics with Pharmacy University. Over 400 participants took Hands-on Training on Cardio-pulmonary resuscitation (CPR) given by Dr. Agarwal.

Workshop on “Invasive and Non-invasive Hemodynamics in Animals”

Workshop on “Invasive and Non-invasive Hemodynamics in Animals” was organized at ICCS-2020 in association with AD Instruments. Around 38 participants from IIT,



IACS-Distinguished Leadership Award in Cardiovascular Sciences was bestowed upon Prof. Ramesh K. Goyal, Conference Chair and Vice Chancellor, DPSRU(R) at the hands of Prof. Randeep Guleria and Prof. N.S. Dhalla (L)

AIIMS, Jamia Hamdard University and many other institutes had attended the workshop. The aim of this workshop was to introduce techniques for measuring invasive hemodynamics parameters.

There was a live demo/hands-on of Pressure-Volume (PV) catheters to provide researchers with cutting-edge technology to record and analyse high-fidelity cardiovascular signals (Pressure, Volume, PV loops). During this workshop, the researchers got the opportunity to examine individual loops, calculate and display End-systolic and End-diastolic PV relationships, to generate multiple plots like Preload-recrutable stroke work (PRSW), dP/dt max vs. End Diastolic Volume (EDV), Pressure-Volume Area (PVA) vs. EDV, PVA vs. End Systolic Pressure (ESP) etc. Workshop was well coordinated by Mr. Aas Mohd from AD Instruments and Dr. Mukesh Nandave, Ms. Megha Sahu and Mr. Sayed Mumtaz from DPSRU.



IACS-Lifetime Achievement Award was bestowed upon Prof. C.C. Kartha, President, IACS-India Section (L) at the hands of Prof. Randeep Guleria and Prof. N.S. Dhalla (R)

The scientific sessions of ICCS-2020 included thought provoking profound lectures on translational research for cardiovascular injuries in the battlefield, medical devices for cardiac care, clinical cardiology cases, artificial intelligence and its applications in CV research, advances



Some conference participants with Prof. R.K. Goyal and Prof. D.K. Agrawal

in nutritional interventions for cardiometabolic diseases. In scientific session on “The Newer Trends in clinical cardiology” there were 5 eminent speakers representing different parts of the world and elaborated on exciting new developments and innovations. This session was chaired by Dr. Lindsay Brown from University of Southern Queensland Australia, Dr. Thomas Jespersen from Department of Biomedical Sciences, University of Copenhagen, Denmark and Dr. Mahesh P Gupta, University of Chicago, USA, who is also a member of Scientific Advisory board in International Academy of Cardiology.

Prof Suresh K Gupta Oration and the Prof Ramesh K Goyal Oration, were conferred to Dr. Lorrie Kirshenbaum and Prof. Buddhadeb Dawn, for their commendable contributions in the field of cell death and stem cell research, respectively by Dr Ram B. Singh, Dept of Biomedical Sciences, Bundelkhand University, Prof. Shailendra Vajpayee, former Principal Government Medical College, Surat and Prof R. K. Goyal, Hon. Vice Chancellor, DPSRU, New Delhi. The Award Winning Orations were chaired by Dr. CC Kartha, President, IACS-India Section.

Riya and Paul Ganguly Symposium in Diabetes: Prof. Sandhya Sitasawad, National Centre for Cell Science, Pune Elaborated on “Redox Regulation in Diabetic Cardiomyopathy: A Journey”. Followed by detail talk on “Role of Early Micro RNA Alteration in Chronic Hyperinsulinemia Mediated Insulin Resistance” delivered by Prof. Anil N. Gaikwad, Central Drug Research Institute, Lucknow. Other speakers of this symposium were Prof. Biju Soman, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Trivandrum (Use of Waist Circumference to Monitor NCD Risk Factors in India: Results from a State-wide Study in Kerala) and Dr. Bhoomika Patel, Nirma University, Ahmedabad (Differential Role of HDAC Inhibitors in Cardiac Complications of Diabetes and Cancer).

The Plenary lectures: These were delivered by eminent speakers of world. Prof. N.S. Dhalla, Institute of Cardiovascular Sciences, St. Boniface Hospital



Workshop on “Invasive and Non-invasive Hemodynamics in Animals” organized in association with AD Instruments

Albrechtsen Research Centre, Canada, talked about Reversal of Cardiac Modelling in Heart Failure with Antihypertensive Drugs. Another plenary lecture on Mitigation of Oxidative/Nitrosative Stress by Vitamin C in Doxorubicin-Induced Cardiomyopathy was delivered by Prof. Pawan K. Singal, Institute of Cardiovascular Sciences, St. Boniface Hospital Albrechtsen Research Centre, Canada This session was chaired by Prof. Raja Babu Panwar and Prof. C.C. Kartha.



Prof. Suresh K. Gupta Oration was delivered by Prof. Lorrie Kirshenbaum, Director, Institute of Cardiovascular Sciences, University of Manitoba, Manitoba, Canada

On 22nd Feb,2020, the second day started with a thunderous applause for the legendary speakers on theme of a scientific session “Prevention of Cardiovascular diseases”. Prof Milind Parle from Guru Jambheshwar University of Science and Technology and Prof D.P Pathak, Director, DIPSAR, chaired the session. The next scientific session on “Clinical Case Study in Cardiology Practice” was chaired by Prof. J.L. Aggarwal, Dean/Director Research and Head of Physiology Dept, Saraswathi Institute of Medical Sciences, Prof J.L Aggarwal and Prof Buddhadeb Dawn, Chairman of the Department of Internal Medicine at the University of Nevada, Las Vegas.



IACS-India Section Distinguished services award to Dr. Mukesh Nandave at the hands of Prof. Dwivedi and Prof. Deka

The next session was on “Cardio Vascular Injuries in the Battle field: Challenges and Translational Research”. The speakers who elaborated on this session were Dr. Aseem Bhatnagar from DRDO, INMAS (Role of NDRF in Saving Lives in Disaster Zones), Dr. H.B. Mohanty, Director & IG, SSB (Basic Management of Chest Trauma in Low Intensity Conflict Area) and Dr. Manju Popli, Additional Director & Head Dept. Of Radiological Imaging INMAS DRDO, Ministry of Defence, Govt. of



Prof. Ramesh K. Goyal Oration was delivered by Prof. Buddhadeb Dawn, Division of Cardiovascular Medicine, University of Nevada, Las Vegas School of Medicine, Las Vegas, USA

India Delhi (Novel Life Saving Products from DRDO for the Battlefield).

The scientific session on Innovations in Medical Devices for Cardiovascular Diseases was chaired by Prof. Manish Diwan, Prof. Sangeeta Bhaskar, Prof. Harvinder Popli and Prof. Vijay Bhalla. A quite informative talk on “India’s Healthcare System: An Overview” was delivered by Prof. Siddharth Bhattacharya, NAT Health, New Delhi. This session was followed by in-depth discussion on “Innovations in Medical Devices used for Cardiovascular Diseases” by Dr. Bharti Khanna, Amarant Lifescience Pvt. Ltd., Delhi. The other speakers of this session who



IACS-India Section Distinguished services award to Dr. Rajani Mathur at the hands of Prof.Dwivedi and Prof.R.C.Deka

joined were Prof. Naresh Bhatnagar, IIT, Delhi (Use Of Biodegradable Smart Materials In Stents).

Prof Rakesh C. Kukreja Oration was delivered by Prof Vandana Patravale, Institute of Chemical Technology, Mumbai on “Innovative and Affordable Drug Eluting



Prof. Vandana Patravale, Institute of Chemical Technology, Mumbai delivered the Prof. Rakesh C. Kukreja Oration

Stents- A Journey from Academic Lab to Patients”. This oration was chaired by Prof. Rakesh C. Kukreja and Prof. Hari Sharma. A plenary lecture on “Allogeneic Stem Cell Therapy for Cardiac Regeneration” elaborated by Prof. Sanjiv Dhingra, Institute of Cardiovascular Sciences, University of Manitoba, Winnipeg, Canada. The chairpersons of this session were Prof. Shridhar Dwivedi, Dr. Devendra K. Agrawal and Prof. H.S. Rehan.

The next speaker Prof. Hari S. Sharma, from VUmc University Medical Center, Amsterdam, Netherlands delivered the lecture on Stunted Angiogenesis And



Mrs. Shakun Goyal was recognized for her enthusiastic support to her husband for organizing successful meeting

Myocardial Fibrosis In Developing Congenital Human Heart Failure: Identifying Therapeutic Targets. A scientific session on Artificial Intelligence and Digital

Health in Industry for Cardiovascular Diseases was chaired by Prof. Vandana Sethi, Ashwani Kumar, Amit Khanna and Poulomi Bhattacharya. A talk elaborated by Prof. Khondaker Abdullah Mamun, CMED Health, BD on “Digital/ mHealth for Personalized Preventive Healthcare and Lifestyle Management” was followed by



Felicitation of Prof. Pawan K. Singal by Prof. Sridhar Dwivedi and Prof. Ramesh K. Goyal

Prof. Kunal Bose, Qure.ai, India (Artificial Intelligence In Medical Imaging Diagnostics And Disease Epidemiology), Prof. Subbash Guddati, Entegris Inc., Singapore (3D Printing In The Pharmaceutical & Health Supplement, Medical Devices & Implants Industries) and Prof. Chandan Mishra, Lodestar 3D, India (Overview Of 3DP/Additive Manufacturers And Hardware Technologies). This scientific session ended with a panel discussion under moderation of Prof. Kunal Bose.

A knowledge rich Symposium on Cellular & Genomic Mechanisms in Heart Failure Molecular Mechanisms was spoken by Prof. Mahesh P. Gupta, University of Chicago, Chicago, USA (Role Of Sirtuins In Protecting Mitochondrial Fitness And Aging Associated Cardiac Remodelling), Dr. Anuradha Majumdar, Bombay College of Pharmacy, Mumbai, Dr. Sanjay K. Banerjee, THSTI, Faridabad (Pregestational Diabetes Impairs Cardiac Function In Neonates: Uncovering). Chairpersons of this session were Drs. Mohammed Zahid Ashraf; Reeta KH and Meenakshi Chauhan.

A scientific session focusing on Molecular Mechanisms in Hypertension was conducted and chairpersons who joined were Prof. Naranjan S Dhalla and Dr. Neeta Kumar. Prof. Suresh C. Tyagi, University of Louisville, School of Medicine, Kentucky, USA gave an insight about “Epigenetic Mechanism of Growth Retardation: A Consequence of Hyperhomocystenemia”. Other eminent speakers of this session were Prof. Surya Ramachandran, Rajiv Gandhi Centre for Biotechnology Thiruvananthapuram (Monocyte Protein Signatures Of Atherosclerosis In Diabetes), Prof. Anita Mehta, L.M.

College of Pharmacy, Ahmedabad (Cardio-Protective Effects Of Gαq-RGS2 Signaling Inhibitor In Experimental Models Of Myocardial Infarction), Prof. S. Sumi, Rajiv Gandhi Centre for Biotechnology,

Oxide by Metal Complexes and Fluorescence Detection of Nitric Oxide by Designed Probes), Prof. Kavita Gulati, Department of Pharmacology, V.P. Chest Institute, University of Delhi (Translational Approach To Abate



Session on “Cardio Vascular Injuries in the Battle field: Challenges and Translational Research” organised and sponsored by Defence Research and Development Organization (DRDO)

Thiruvananthapuram (Molecular Pathogenesis Of Varicose Veins), and Prof. Suman Kundu, Department of Biochemistry, University of Delhi, New Delhi (Drug Discovery Initiative To Combat Hypertension: A Heartening Story).

On 23rd Feb, 2020, scientific session on recent trends in cardiac devices and stents chaired by Dr. Rajiv Taliyan. Dr. Rajiv Agarwal from Max Smart Super Specialty Hospital, Saket, Delhi spoke on “Advances in Pacemaker Technique and Technology (Leadless Pacemaker)” followed by elaborate talk entitled “Role of Antiplatelet Drugs in Cardiac Care” delivered by Dr. Ganesh Kumar Mani from Max Smart Super Specialty Hospital, Saket, Delhi. Other speakers of this session were Dr. Ripen Gupta, Max Smart Super Specialty Hospital, Saket, Delhi (Drug-eluting Stents and Steroid-eluting Pacemaker Leads), Dr. Rahul Chandola, Max Smart Super Specialty Hospital, Saket, Delhi (The Angiotensin Receptor Neprilysin Inhibitor (ARNI) In CHF).

A symposium on Nitric Oxide in Cardiovascular Diseases was conducted by Society of Nitric Oxide. The chairpersons of this symposium were Prof. Md. Iqbal Alam, Prof. Sayeed Ahmad and Prof. Roop K. Khar. They were joined by eminent speakers of different parts of India Prof. Arunaba Ray, Hamdard Institute of Medical sciences, New Delhi (The Translation Of Nitric Oxide Research To Therapeutics: An Overview), Kaushik Ghosh, IIT, Roorkee (Photo-induced Donation of Nitric

Theophylline Induced Cardiotoxicity), Dr. Madhu Dikshit, National Chair, THSTI, Faridabad (Neuronal Nitric Oxide Synthase: A Critical Regulator Of Neutrophil Differentiation), and Suvro Chatterjee, AU-KBC, Chennai (An Ex-Vivo Study Of Atherosclerotic Plaque And Its Impact On Adjacent Endothelium).

Prof. Harpal Buttar Oration was delivered by Dr. Atul Abhyankar, from Mahavir Heart Institute, Surat, on “The Journey of Indian Drug Eluting Stent- Swimming Against the Tide”. The chairpersons of this oration were Prof. Harpal Buttar, Prof. Ramesh K. Goyal and Dr. Mukesh Nandave. A panel discussion on Pharmacovigilance and



Prof. Harpal S. Buttar Oration was delivered by Dr. Atul Abhyankar, Mahavir Heart Institute, Surat, Gujrat

Regulations of Cardiac Devices was conducted and joined by eminent speakers Dr. Jai Prakash, IPC, Ghaziabad, Dr. Khalid Khan, Fermish Clinical Technologies Pvt. Ltd., Dr. Sumati Randeo, Roche Diagnostics India Pvt. Ltd. and Dr. Vivek Singh. Clinical Cardiology Case studies

Research Institute of the Council of Scientific and Industrial Research and Dr. Manish Lavhale, Associate Director of Research and Development at Pharmazz, Inc, India. Followed by the next session was to visualize “Advances in Nutritional Interventions for Cardio



Session on Molecular Mechanisms in Hypertension was conducted and chaired by Prof. Naranjan S Dhalla, Prof. N. K. Ganguly, Dr. Neeta Kumar and Prof. Suresh C. Tyagi

were addressed by Dr. Thomas Jespersen, Department of Biomedical Sciences, University of Copenhagen, Denmark entitled “Ventricular Fibrillation During Acute Myocardial Infarction- Lessons From A Pig Model”. This scientific session was chaired by Prof. Surender Singh, Prof. Prabhat K Sahoo, Prof. Abul Kalam Najmi, Prof. V. Madhuri and Prof. Kirti. Other speakers were Dr. Shyam S. Sharma, NIPER, Mohali (Elucidation of Role of Protease Activated Receptors (PARs) in Diabetes-induced Cardiac Dysfunctions using Pharmacological Approach), Dr. Harlokes N Yadav, AIIMS, Delhi (Conditioning of the Heart: Update), and Dr. Ekta Kapoor, Dept. of Science & Technology (DST), Delhi (Application of GLP in the Outcome of Cardiovascular Research).

Scientific session on “New Targets in Treatment of cardiovascular disease”, which was chaired by renowned chairpersons on stage Dr Surya Ramachandran an Indian Cardiovascular biologist and Director Central Drug

Metabolic Diseases”, to abreast & address the rising needs of the public and was chaired by Dr Tanveer Naved, Joint Head & Associate Professor in Amity Institute of Pharmacy and Prof. Rajiv Kumar Tonk from Department of Pharmaceutical Chemistry, DPSRU, and Prof Kanchan Kohli, Professor, Department of Pharmaceutics, Jamia Hamdard.

Proceeding towards the end of this International Conference, the **valedictory function** was organised in the august presence of Dr. Dhananjay Sable, Assistant Drug Controller and representative of Chief Guest, Dr. V. G. Somani, DCGI, CDSCO, New Delhi. The Guest of Honour of the valedictory function was Dr. N. Subramanian, Director, Indraprastha Apollo Hospital, New Delhi. Total 25 awards were given to best oral and poster research paper presentations in the name of Prof. N.S. Dhalla, Prof. N.K. Ganguly, Prof. C.C. Kartha, Prof. Suresh K. Tyagi and Prof. D.K. Agrawal.

Academy Honours Dr. R.B. Panwar with IACS Fellowship



Dr. Raja B. Panwar

Dr Raja Babu Panwar is an Indian Cardiologist who is presently Vice Chancellor of Rajasthan University of Health Sciences (RUHS), Rajasthan, India. Over the past 4 decades, he has been actively engaged in teaching and research in clinical cardiology as well as in administration of medical education. His

dedication and commitment for improving cardiovascular medicine throughout India are commendable. The Academy bestowed its Fellowship Award upon Dr. Panwar at a special ceremony in New Delhi during February 21-23, 2020. The following is a record of his achievements:

Academics

Graduation and post-graduation from SP Medical College, Bikaner, Rajasthan, India in 1976 and 1979, respectively. Thereafter, DNB (Cardiology), National Board of Examination, New Delhi in the year 1993. Fellowship in

cardiology in AIIMS, India; GB Pant New Delhi, India; University of Virginia USA, Australia (WHF)

Administrative Experience

- Posts held as Head Cardiology Department, Superintendent and Principal, SP Medical College, Bikaner during the period 1996-2012.
- Pro Vice Chancellor, RUHS, Jaipur.
- Member PG Committee of Medical Council of India (MCI), New Delhi, India.
- Member, Board of Governors of MCI, New Delhi, India.

Academic Record:

- Published more than 150 research papers in national and international journals of repute including Lancet, New England Journal of Medicine, American journal of Cardiology, European Heart Journal, API, Echocardiography, Indian Heart Journal, JAMA, etc.
- Member of editorial board of leading academic journals.
- Visiting faculty of Mount Sinai, USA ; Saint Peter University Medical College, USA.
- Subject expert and examiner at various Universities.
- Actively organised various workshops and conferences.
- Worked as research scholar with financial assistance and collaboration of Indian Council of Medical Research, New Delhi; All India Institute of Medical Sciences; St John's Medical College, Bangalore, India, Mac Master University of Canada, Duke University of USA, Mount Sinai School of Medicine, NY, USA, World Heart Federation & various industries.
- Patent-(1) A novel fumigation methodology for antibacterial action (2) The SEPRDD-CHF: A JVP guided diuretic releasing system for patients with acute precipitation over congestive heart failure.

Awards /Honors

- Recipient of many awards/ honors including district award by Collector of Bikaner in 1993 and State award of 2003 conferred by Honorable Governor of Rajasthan for outstanding Medical services.
- Member of delegation of State of Rajasthan visited USA and as member of delegation of Government of India to visit Russia, Armenia and Georgia.
- Participated in European Commission meeting for financial grant of Malaria research in Spain.
- Best poster award (from India) at the meeting of American College of Cardiology (USA).

Unique Achievements

- Introduced first mobile cath lab in India (which was flag-off by President of India).
- Publish unique entity Subclinical carditis in asymptomatic school children by Echocardiography which has been finally incorporated in World Heart Fedration criteria and incorporated in Jones Criteria of Rheumatic Fever.
- Investigator of various international and national researches viz. The RE-LY Atrial Fibrillation Registry, ARISTOTLE Trial, Creat Ecla, Oasis 5,6, PURE, Umpire, Poise, Early ACS, Vitatops, Rocket AF, Averroes, RE-LY Atrial fibrillation, study on the RHEUMATIC Acturial trends in Indian population and having many publications with above 36,449 citations in leading national and international journals of repute. These researches have contributed to important scientific findings and few have been incorporated as guidelines / regime for treatment in the field of non-valvular atrial fibrillation and non ST elevation of Myocardial infarction.
- Key person to start new medical college in Jaipur (RUHS College of Medical Sciences), develop RUHS as an independent university and also developed 500 bedded hospital (406 crores INR).
- Pioneer to start skill upgradation course in Medical & Dental colleges of Rajasthan.
- Established Chair in Bioethics of UNESCO in RUHS.

Philanthropic and Social Activities

- Motivated various philanthropic agencies and social trusts generating about INR 50 crores to equip various hospitals and build colleges.
- Organised special camps of pediatric cardiology, electrophysiology, cardiac surgery, interventional cardiology with assistance of national and international faculty.

Extracurricular Activities

An active player of table tennis and won various State and National Titles.

Social Service

Adoption of village Ajmeripura and converting it to SMART Village by creating various facilities including supply of pure water, health sub center, starting adult education, introducing M and e health system for village, plantation and digging, creating computer and e learning centre facilities.

Academy Bestows a High Honour to IACS-India Section President



Dr. C.C. Kartha

Chandrasekharan Cheranellore Kartha (born 1951) is presently Honorary Senior Adviser for Society for Continuing Medical Education & Research at Kerala Institute of Medical Sciences at Trivandrum, India. Immediately before joining this position, he was Honorary

Distinguished Professor of Disease Biology and

Molecular Medicine at Rajiv Gandhi Center for Biotechnology, an autonomous institute under the Department of Biotechnology, Government of India. He was earlier Senior Professor and founder Head of the Division of Cellular and Molecular Cardiology at Sree Chitra Tirunal Institute for Medical Sciences and Technology, an Institute of National Importance under Department of Science and Technology, Government of India. He also served as the Dean of academic affairs of the Institute in the years 2000-2003.

He is the current President of the Indian Section of International Academy of Cardiovascular Sciences. He is also Chairman of the Advisory Committee for the Multidisciplinary Research Unit at Government Medical College, Trivandrum.

Kartha has an outstanding record as a cardiovascular pathologist and as a serious investigator in cardiovascular disease biology. His contributions to the understanding of molecular basis of diseases have received acclaim among physicians and scientists alike over the years. A notable feature of his research is the distinct emphasis on questions directly related to mechanisms of human cardiovascular diseases. He has employed tools of cell biology, biochemistry, physiology, pharmacology, molecular biology, experimental cardiology and epidemiology for his pursuits. He has thus been able to provide a link between basic sciences and clinical cardiology to the young investigators he has trained.

Kartha graduated from Trivandrum Medical College in the year 1974 and took his MD degree in Pathology from All India Institute of Medical Sciences, New Delhi in

1979. He joined Sree Chitra Tirunal Institute in its formative years as Lecturer in Pathology and rose to the position of Additional Professor of Pathology in 1988. He was responsible for organizing and leading the cardiac pathology services and an electron microscopy laboratory in the Institute. He was also associated with the early stages of development of disposable blood bags, dental materials and a large diameter vascular graft. In 1993, he was appointed as the Professor and head of the then newly created Division of Cellular and Molecular Cardiology, an interdisciplinary group for cardiovascular research. He is credited with organizing the first Molecular Cardiology division in India.

During the early part of his career, his focus was to delineate the cause of endomyocardial fibrosis, a tropical cardiomyopathy. His studies disengaged the aetiopathogenesis of the disease from a confusing network of hypotheses and placed it in the context of a geochemical cause with the primary tissue response being interstitial in nature. Kartha has evaluated through experimental and epidemiological studies, the geochemical hypothesis proposed by MS.Valiathan and Kartha. His studies on endomyocardial fibrosis spurred his interest in the biology of cardiac endothelium and he has made original contributions to the current understanding of the role of endocardial endothelium in the regulation of cardiac function and in cardiac remodeling secondary to cardiac failure.

In 2009, Kartha was invited by Rajiv Gandhi Centre for Biotechnology as Professor of Eminence to initiate translational cardiovascular biology and establish a division of cardiovascular disease biology at the Centre. He has established a most comprehensive interdisciplinary laboratory for cardiovascular research at Rajiv Gandhi Centre, where he also initiated research on a broad range of clinically relevant themes which include, cardiac stem cell biology, vascular disease in type 2 diabetes, hereditary basis for varicose veins, molecular pathogenesis of cerebral arterio-venous malformations, and endothelial remodeling in cardiac failure. These efforts have led to identification of cyclophilin A as a biomarker for vascular disease in type 2 diabetes and the discovery that Forkhead box C2 promoter variant c.-512C.T is associated with increased susceptibility to varicose veins. Another interesting work of his is the finding that chronic pressure overload results in deficiency of mitochondrial membrane transporter

ABCB7 which contributes to metabolic shift and worsens cardiac function. He has also made forays into the emerging discipline of Ayurvedic Biology. His studies have demonstrated that a rejuvenating medicine prepared from *Phyllanthus Embilica* enhances cardiac mitochondrial and contractile functions and improves cardiac function.

Kartha is an elected Fellow of Royal College of Physicians, London, International Academy of Cardiovascular Sciences (Canada), National Academy of Medical Sciences (India), Indian Academy of Sciences, National Academy of Sciences (India) and Indian College of Pathology.

He has served in the Council of Indian Academy of Sciences, editorial boards of several peer reviewed international journals and on several national and institutional committees.

He has received Makoto Nagano Award, Ramesh K Goyal Oration Award and Distinguished Leadership Award from International Academy of Cardiovascular Sciences. He is also a recipient of Manjeet Singh Oration

Award from Indian Section of International Society for Heart Research.

Kartha has published more than 136 articles in peer-reviewed journals, authored a book, edited 5 books and focussed editions of 2 journals, authored 17 reviews and contributed chapters in 20 books. He has also authored several popular science articles for vernacular magazines and a chapter on Medical Technology for an illustrated Encyclopedia on Technology published by Kerala State Institute of Children's Literature. Professor Kartha is married to Dr. Mira Mohanty, a pathologist who retired as Senior Scientist and Associate Head of Biomedical Technology Wing of Sree Chitra Tirunal Institute of Medical Sciences and Technology.

Dr. C.C. Kartha was honoured by the Academy with Lifetime Achievement Award at a special ceremony held in New Delhi during February 21-23, 2020. Dr. Kartha, from Trivandrum is the current President of the IACS-India Section and has been committed to promote the scientific basis for the practice of cardiovascular medicine as well as young investigators in India. While accepting this Award, he gave the following speech.

Acceptance Speech by Dr. C. C. Kartha

Indeed, this award is a great honour for me. I am grateful to the members of the Council of International Academy of Cardiovascular Sciences for bestowing me this recognition. Certainly, I would cherish this souvenir for ever.

I started my career more than forty years ago, as a Tutor in the Department of Forensic Medicine at my alma mater, the Government Medical College at Trivandrum. I had no idea at that time about my professional trajectory. My passion then was to grasp the causes and mechanisms of human diseases and even today it stays unchanged. Though my parents were to some extent disappointed that I was not inclined to pursue clinical medicine, they supported my choice of Pathology for specialization. I was fortunate to have my training at the All India Institute of Medical Sciences, the number one medical school then and even now.

I have immensely enjoyed my life and the 40 years of pursuit of my interests. Several people have contributed to this success: primarily, my parents who opened my eyes to the world of books and nurtured my interest in everything under the sun. A broad interest has helped me chase causes and mechanisms not only of diseases, in which I specialized but also of transitions in human life and history, society and different forms of art.

I have had the benefit of learning from a large number of my professional colleagues and students and also of collaborating with many of them who were more talented and skilled than me. They helped me to exploit domains other than my own speciality for my investigations related to human diseases. I am grateful to all of them.

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2002 was the year when I first met Professor Dhalla and was introduced to the International Academy of Cardiovascular Sciences. The Academy has been a great influence on me since then. Meetings of the Academy provided opportunity for me to meet, hear and interact with several senior and young leading creative investigators in cardiovascular science, who have fostered

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I thank all of you for being here and enriching my moment of joy and pride.

I also bow down to the formless, sans attributes, immutable, unknown, unknowable and omnipresent Absolute.

Drug induced QT Interval Prolongation Risk Factors for Female Patients Undergoing Current Treatments for COVID-19

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Investigational drugs chloroquine, hydroxychloroquine, remdesivir and lopinavir-ritonavir are being assessed for their potential to slow COVID-19 disease progression or improve survival ^{1,2}. Anecdotal clinical data also suggests elevated efficacy of hydroxychloroquine treatment in combination with azithromycin for hospitalized COVID-19 patients ^{3,4}. The severity of the pandemic and absence of approved drugs has promoted widespread off-label prescription of these investigational pharmacotherapies.

Lopinavir-ritonavir has not show promise for treatment of hospitalized COVID-19 patients with pneumonia in a recent clinical trial in China ⁵. Remdesivir being a new investigational antiviral drug has unknown safety profiles. The remaining three investigational drugs: chloroquine, hydroxychloroquine and azithromycin are all individually implicated in prolonging corrected heart rate (QTc), a measure of QT prolongation and a predictor of the fatal arrhythmia torsade de pointes (TdP) ^{6,7,8,9}. TdP risk has resulted in removal of 14 prescription drugs from the marketplace ¹⁰.

Concurrent use of two or more drugs with QT interval prolongation potential can cause additive increased risk of ventricular arrhythmias and sudden death. Although no toxicity has been reported with short term use of these drugs, the possibility of synergistic arrhythmic effects of the current COVID-19 combination therapy cannot be overlooked ^{11,12,13,14}. This becomes even more important for female COVID-19 patients as female sex is one of the highest pro-arrhythmic risk factor that significantly increases susceptibility to cardiotoxicity on exposure to drugs that induce QTc prolongation ^{15,16,17,18}. Female

participants focused QTc/cardiac monitoring should be an essential outcome measures in all study designs evaluating any combinations of these drugs. Some factors potentiating higher cardiac toxicity risks in females are discussed here.

Higher Propensity for Acquired LQTS and Drug Drug Interactions

Female gender has been increasingly recognized as an independent risk factor for drug induce long QT syndrome DI-LQTS ¹⁹. TdP occurs three times more commonly in women than in men ¹⁸.

Acquired LQTS mainly occurs on exposure to an environmental stressor, most common being an adverse drug reaction which can lead to DI-LQTS. Underlying mechanism for DI- LQTS almost exclusively involves the reduction of IKr through human eether-à-go-go related gene (hERG) potassium channel blockade ¹⁹. DI-LQTS has been, for decades, one of the most common causes for withdrawal of drugs from the market.

The QT interval prolongation relative to the administration of IKr blockers is greater in women and accompanied by a propensity of drug-induced polymorphic ventricular arrhythmia ²⁰. The estrogen-mediated reduced repolarization reserve in women is believed to be responsible for their higher susceptibility to DI-LQTS ¹⁹. Administration of more than one drug that prolong repolarization increases the risk of DI- LQTS. In most cases, the mechanism of increased risk is due to drug-drug interactions altering metabolism, rather than simple additive effects changed cardiac currents.

Cytochrome P450 superfamily of proteins is responsible for the metabolism of most of the drugs by liver, CYP3A4 being the predominant cytochrome. Coadministration of drugs which are substrates for CYP3A4 and, also blockers of the inward potassium rectifier IKr results in further risk escalation for QT prolongation. Chloroquine, hydroxychloroquine and azithromycin are all cytochrome P-450 CYP3A substrates and prolong QT interval by inhibiting cardiac potassium channels encoded by hERG as shown in Table 1.

Drug	Cytochrome Isoform	Potassium Channel
Chloroquine	P-450 CYP3A substrate	Inhibits IKr (hERG)
Hydroxychloroquine	P-450 CYP3A substrate	Inhibits IKr, If & ICaL channels <i>Blockade of ICaL could be countering some of the effect of the hERG channel block, HCQ associated cardiac arrhythmia not reported</i> ²¹
Azithromycin	P-450 CYP3A substrate	Weak IKr (hERG) blocker
Hormones/ OCs (4th Generation)	Metabolized by Cytochrome P450	Estrogen inhibits IKr & IKs channels, partially suppresses hERG currents

Females using oral contraceptives (OCs) have another risk tier added. OCs are mostly cytochrome P-450 CYP3A substrates and inhibit hERG potassium channels. All listed current COVID-19 pharmacotherapies are CYP3A4 substrates and block cardiac voltage gated potassium channels, particularly the rapid component (IKr) of the delayed rectifier potassium current (IK). Short term concomitant administration of these drugs that inhibit cytochrome P450 and prolong the QT interval may be warranted only in a monitored setting in absence of other alternatives.

Greater Genetic Predisposition for LQTS

Women also have a higher predisposition to genetic mutations that potentiate TdP. Long QT syndrome is one of the most common genetic arrhythmia syndromes. Congenital LQTS is caused by mutations in the genes encoding potassium and sodium protein channels (IKr, IKs and Na) that lead to increase or decrease of their associated currents^{22,23,24,25}.

Mutations in 13 genes are associated with congenital LQTS of which, mutation in 3 genes, LQT1, LQT2, and LQT3 account for around 75% of all cases of clinically definite LQTS and 95% of genetically identifiable LQTS^{26,27,28,29,30}. LQT1 is caused by mutations in potassium channel gene KCNQ1 (KVLQT1) and accounts for 40–55% of cases of the LQTS^{31,32}. LQT2 accounts for 35–45% of cases of congenital and is caused by mutations in potassium channel gene KCNH2 (also known as hERG). LQT3 accounts for 8–10% of cases and is caused by mutations in the sodium channel gene (SCN5A)^{31,32}.

Women are at higher risk than men of TdP with LQT type 1 and type 2 (LQT1 and LQT2)³³. Women with the LQT2 genotype more likely to experience a cardiac event during pregnancy than women with the LQT1 or LQT3 genotype^{32,34}. The postpartum high-risk can be reduced by using beta-blocker therapy³⁵.

Additionally, congenital LQTS may have an incomplete penetrance due to subclinical mutations³⁶. These patients are asymptomatic but more susceptible to QT prolongation and TdP, when exposed to QT prolonging agents^{36,37}. Most likely, subclinical mutations also contribute to the greater genetic predisposition as well as higher propensity for DI-LQTS in women.

Baseline QTc Alterations

Women have a longer QT_c than men^{38,39,40,41,42}. Additionally, the timing, dispersion, and morphology of the T wave is also different^{42,43,44,45,46}. The resting RR intervals, are shorter and women have higher vagal tone and lower heart rate variability than men^{47,48}. The QT-to-RR ratio is also steeper in women than in men^{45,50}, with the result that at slower heart rates, sex differences are more pronounced and the QRS complex shorter in women than men⁵¹. The underlying molecular mechanisms for differences in the electrical profile are largely unknown. The absence of QT_c variance in neonates and manifestation around puberty, co incidental with sex hormone surge, implicates a hormonal mediated differentiation in cardiac electrical activities.

QT_c interval values between 350-440 ms are considered normal. Values between 440-460 ms and 440-470 ms are considered borderline in men and women, respectively. Above these values the QT-interval is considered prolonged⁵². However, arrhythmias are more frequently associated with values above 500 ms⁵⁴. The risk for TdP increases as particularly as QT_c interval exceeds 500 ms. These collectively present marked differences in QT intervals of men and women including a longer QT_c. Even a small 6–10 ms increase QT_c is clinically relevant and considered a risk by FDA and 10 ms increase has been linked with a 19% increase in SCD⁵³. Although the underlying molecular mechanisms for differences are

largely unknown, the absence of QTc variance in neonates and manifestation around puberty implicates a hormonal mediated differentiation in cardiac electrical activities ⁵⁴. The QTc interval is shaped by both endogenous and exogenous sex hormones as described below.

Endogenous Sex Hormones and QTc

Menstrual cycle. Conflicting results of the hormonal fluctuations observed during a single menstrual cycle on the QT interval have been reported.

- Endogenous estrogen lengthens the QTc interval in animals ⁵⁵.
- Endogenous testosterone and progesterone shorten the action potential ⁵⁶.
- Complex QTc regulation by sex steroid hormones involving gonadotropins.
- Protective effect of the luteal phase (438±16ms) compared to menstrual (446) and follicular (444) phases on DI QTc prolongation ⁵⁷.

Current consensus is that menstrual cycle hormonal variations do not trigger QTc changes *in vivo* unless medications with cardiac repolarization and QTc alteration capabilities are co-administered. In healthy volunteers, drug induced (DI QTc) interval lengthening is greatest during the menses and ovulation phases and least during the luteal phase.

Pregnancy. QT interval in pregnant women stays in normal, albeit slightly longer range compared to non-pregnant women. As discussed under “Greater Genetic Predisposition for LQTS” section above, females with supraventricular arrhythmias present increased symptoms during pregnancy ⁵⁸. In pregnant women with LQTS the 9-month postpartum period is associated with a 2.7-fold increased risk of experiencing a cardiac event and a 4.1-fold increased risk of experiencing a life-threatening event when compared with the preconception time period ⁵⁹. Clinicians and patients need to factor the heightened LQTS risk nine months post pregnancy during treatment and consider appropriate monitoring of these patients.

Exogenous Sex Hormones and QT Interval

Oral Contraceptives. QTc might be influenced by the androgenicity of oral contraceptives (OCs) in women (4). OC users have a shorter QTc than nonusers. Four generations of OCs by progestin type have been developed. First and second-generation OCs have progestins that are androgenic with relatively high levels of estrogen. The third generation OCs have progestins that are less androgenic while the fourth generation OCs are non-testosterone derived and antiandrogenic ⁶⁰. OC generation is an important predictor of QTc length alteration. First and second-generation OC users have a

shorter QTc while fourth generation OC users have a longer QTc.

Almost 4 ms longer QTc (403.5 ms) has been reported amongst fourth generation OC users as compared to first (400.8 ms), second (399.2 ms) and third generation (400.8 ms) OC users ⁶¹. The effect of OC on the QTc is not modified by estrogen dose. Additionally, OCs use also potentiates drug induced TdP (DI-TdP) in females as described earlier.

Emergency Contraception. Emergency contraceptives (ECs) are progestin based or a combined regimen of estrogen and progestin with similar effects on QTc as describes above. CYP3A is the major enzyme for oxidative metabolism of progestin based or estrogen and progestin combined regimen ECs. Strong inducers of CYP3A4 may reduce the effectiveness of ECs containing ulipristal, progestin only, or a combination of ethinyl estradiol and a progestin.

Menopause hormone therapy. In general, Menopause hormone therapy uses doses of estrogen and progesterone that are 5–10-fold lower than OCs. This translates into similar but very attenuated response reported by OC use. Studies of menopausal hormone therapy (MHT) in the form of estrogen-alone therapy (ET) and estrogen plus progesterone therapy (EPT) have suggested a counterbalancing effect of exogenous estrogen and progesterone on the QT ⁶².

Acne and premenstrual dysmorphic medications. The fourth generation OCs are currently also approved and in widespread use for non-contraceptive indications like acne and premenstrual dysmorphic disorder. Since 4th generation OCs are associated with QTc lengthening and associated cardiovascular risks, possible discontinuation of OCs while receiving COVID-19 pharmacotherapy might be warranted.

Conclusions

Co-administration of multiple QT prolonging and hepatic cytochrome P450 inhibitors along with in a background of female sex related risk factors during the combinatorial treatment could result in concomitant cardiotoxicity risk exposure. Cardiac toxicity has been reported with use of some combination of these of drugs while other combinations showed no acute toxicities ^{11,12,13,14}. Recent reports on use of these drugs in COVID-19 patients do not report sex based QTc as an outcome measure. DI- QT prolongation is an important metric of drug safety. However, the outcome of the associated risks remains unpredictable and individual benefit/ risk assessment is required for each patient. Short-term administration in absence of other alternatives in a monitored setting may be warranted ⁶³. Gender based electrical difference should

be a carefully monitored parameter in study designs of all clinical trials/studies evaluating any combinations of these drugs.

Not only the clinicians, but also the COVID-19 female patients undergoing treatment should be adequately informed about these sex difference elicited risks to ensure compliance to stringent risk mitigation frameworks for safest treatment outcomes.

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We Are What We Eat- Nutrition, Immunity and Virus

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“Healthy nutrition and right lifestyle can get us going”

With no vaccine and drug out there yet, how are the COVID-19 patients recovering? They do fight a good battle with this bad bug but are proven victorious because of their immune system which fought back. Immune system comprising of fighter immune cells are the most important cells in our body to fight any invasion by the foreign beings. Although how quickly and aptly they will revert back really depends on how we have taken care of them, with asymptomatic carriers being the right example.

Can we fight with this virus?

Yes, Human genome which is 1 billion base pairs in length definitely has the ability to fight with SARS-CoV 2 (causing COVID-19) which is 30000 base pairs in length, provided our immune system interferes with its multiplication.

Cell Mediated Immunity

Many infectious microbes invading the host cell or immune cells resists the elimination by host humoral

immune mechanism. This inability of humoral Ig to neutralize intracellular parasites triggers the activation of T lymphocytes which are important in recognizing foreign antigens on the surfaces of host cells. The T-cell derived signaling molecules modulating cytokines production act as saviors in killing the bug as well further potentates in reducing the spread of virus particles to neighboring host cells by releasing IFN- γ (1). Right and healthy nutrition not only triggers the innate immune response to the viral attack but does stimulate the activation of effective immunologic memory.

Inflammation

Inflammation is an importantly coordinated yet complex response by the host's innate immune system to eliminate foreign materials and to facilitate tissue repair. This non-specific response to injury in which phagocytic cells, neutrophils, macrophages, endothelial cells and platelets play an important role is also evident in atherosclerosis. Disruption of endothelial cell function aids in the

localized accumulation of inflammatory cells. Once the process begins with immune cells adherence, it is followed by plaque development. Dyslipidemia will further worsen the situation. Higher the LDL levels more is the plaque formation but higher HDL will play an imperative role in modifying its formation and development (2). Atherosclerosis which was once thought to be disease of just bad lipid profile is now considered to be initiated by inflammation, which plays a major role in its development. This explains why COVID-19 patients with generated inflammatory responses and pre-existing conditions (obesity, hypertension, CVD, diabetes, other metabolic disorders) are highly vulnerable victims.

Nutrition and the ability to fight

Virus infected patients who are immunocompromised, don't have the same innate or adaptive immunity to fight infection and those with pre-existing heart conditions are one of the facile victims. Although It is very well supported by literature that suppressed immune responses are direct outcomes of nutritional deficits. This is very obvious, since metabolic pathways (both anabolic and catabolic) in the immune system just like other physiologic activities are highly dependent on same kind of building blocks and energy sources, with exception of lipids. Immunosuppressed state is likely the result of excess fatty acids and certain shifts in the balance of lipid types.

- **Protein-Calorie Malnutrition (PCM)**

While PCM is the major cause of immunodeficiency, moderate calorie intake is associated with higher T-cell functions (1,3).

- **Protein and Amino Acids**

Feeble tissue repair and decreased resistance to infections is the obvious outcome of Insufficiency in overall protein intake. Arginine and Glutamine are important amino acids in the apt functioning of immune system. While T-lymphocytes in culture are dependent on L-arginine for growth and function, glutamine on the other hand act as an energy source for lymphocytes and macrophages (4,5).

- **Nucleic Acids**

Different cell-mediated immunologic mechanisms are dependent on the availability of purines and pyrimidines in the diet (6). Feeding diets containing preformed nucleotides to critically ill patients have resulted in shorter hospitalization (7).

- **Minerals**

Copper- Copper deficiency has been associated with aggravated infections which may result from impaired phagocyte function and T-cell numbers (8,9). **Iron-** Due to complexities involved with Iron metabolism, reduction in Fe concentration results in decreased T-cell numbers but increase in the activity

of other immune function parameters (8, 10).

Manganese- Act as a component of several metalloenzymes involved in immune functions (11).

Selenium- Apart from being an essential component of an antioxidant enzyme (glutathione peroxidase), Se deficiency take a major halt on immune function suppressing variety of immunologic endpoints (12).

Zinc- Zn deficiency results in number of T-cell abnormalities and lack of response to mitogenic stimuli causing several irregularities in immune system (8, 13).

- **Vitamins**

Vitamin C, A, B-complex, Vitamin D and E are all involved in regulation of immune system by acting as an important factor in an array of metabolic processes regulating gene transcription, enzymatic and redox reactions. Their role in T-cell activities and their function as an antioxidant is an imperative feature protecting the host cell after parasitic or viral invasion (8, 12,14,15).

- **Lipids**

Although fatty acids play a crucial role as cell membrane components, energy source and cell signaling mediators, the type of fatty acids in diet play an imperative role in determining overall immune health. Poly unsaturated fatty acids (PUFA), especially the Essential fatty acids (EFA) n-3 and n-6 have an important role in synthesizing various eicosanoids promoting the proliferation of lymphocytes. On the other hand, having saturated fats in diet and overall increasing consumption of dietary fats results in immunosuppression (16).

- **Carbohydrates**

Polysaccharides as opposed to simple sugars having a low glycemic index can activate or enhance immune responses in macrophages (17).

- **Antioxidants and Plant Derived Phenolic compounds-**

Nutritional compounds (vitamins, trace elements) acting as an antioxidant serve as super foods by promoting oxidant balance and immunity. The role of dietary antioxidants in inflammation, redox related events on different lymphocyte subsets is crucial (18). Apart from vitamins and minerals, various bioactive compounds in fruits and vegetables shows a promising effect as immune system boosters. Polyphenols present in plant sources inhibit lipid oxidation while promoting carbohydrate oxidation. β -Sitosterol, analoe emodin and hesperetin exhibited anti- SARS coronavirus 3C like protease effects, proven by a research study (19).

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Is Ambient Space a Determinant of Human Health?

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"Emptiness which is conceptually liable to be mistaken for sheer nothingness is in fact the reservoir of infinite possibilities." – Daisetz Teitaro Suzuki

The World Health Organization defines health as 'a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity'. Mental and physical well-being are linked to

‘spiritual health’, ‘emotional health’ and ‘financial health’ because of shared association with lower stress levels. The predominant determinants of health are genetics, social, economic and physical environment, nutrition, lifestyle and access to health services. Several determinants of health in the physical environment are known and these include pollutants in the air, water, soil, and food, natural and technological disasters, climate change and occupational hazards. Another factor which influences living organisms is the external milieu which could be the surrounding atmosphere, water or vacuum. Studies on function and dysfunction of humans have centred mostly on the physical body and to a lesser extent on the environment. We propose that the three-dimensional space around individuals could also be a target for intervention to maintain health.

The term ‘space’ is generally used in the context of outer space. The English word ‘space’ is derived from the Latin word for expanse – spatium (room, area, distance, stretch of time) and from the French word espace (period of time, distance and interval).

Interestingly, the existence, form and attributes of space have been deliberated from ancient times. We can find them mentioned in treatises such as Plato’s *Timaeus*, the *Physics* of Aristotle, in Socrates’ reflections on what the Greeks called *khora* (i.e. space) and in the *Discourse on Place* (*Qawl fi al-Makan*) of Alhazen, the 11th century Arab polymath. Ancient Eastern philosophers thought that life originated from space and remarked that awareness preceded the manifestation of space. According to them, we have space in the Universe on lease and when we perish, the physical body goes to the earth space and emotional body enters the vastness of space. These then are the building blocks for another life to blossom.

Rene Descartes defined space (Cartesian space) as Euclidean in structure – infinite, uniform and flat – and containing matter. Matter by definition had a spatial extension; thus, space is not void. Gottfried Leibniz, a German philosopher–mathematician perceived space as a collection of relations between objects. For Isaac Newton, space was absolute with an invariable and independent existence, irrespective of whether there was any matter within. The German philosopher Immanuel Kant opined that the concepts of space and time are part of a scheme that humans own and use to organize all experiences. He indicated that the experience of ‘space’ is ‘pure a priori form of intuition’, and hence subjective.

The concept of space has been central to understanding the physical universe. Space is one of the fundamental quantities in physics, similar to other fundamental quantities such as time and mass. Modern physicists consider physical space with time to be part of a limitless four dimensional continuum known as space–time. It appears that space was created 13.8 billion years ago, in the Big Bang. Space is known to be expanding rapidly because of cosmic inflation.

There are different classes of spaces. Modern mathematicians define space as sets, commonly described as different types of manifolds. Geographical space is land which has an impact on human and cultural behaviour. It is an important factor in architecture, the design of buildings and structures. The term ‘public space’ denotes land collectively owned by a community, while private space is the land owned by an individual for his/her own use and pleasure. In the social sciences, space has been studied from several perspectives such as Marxism, feminism, postmodernism, postcolonialism, urban theory and critical geography. In his book *The Production of Space*, Henri Lefebvre discusses the several overlapping social processes that produce space. In *Third Space*, Edward Soja addresses the binary way in which humans understand space – either physical or as imagined. Lefebvre argues that spatiality is an integral and neglected aspect of how we inhabit, experience and understand the world.

All of us are specific about the spaces we inhabit. We build our habitats for not only living, but to provide us emotional satisfaction as well. We recognize private space, personal space, professional space, social space and spiritual space. Awareness of the living space of a person is critical to safeguard long-term survival, similar to the ecological niches that are relevant to the survival of different species of life. Awareness of the surroundings was important for survival of our ancestors, in relation to hunting, self-preservation as well as conceiving personal space. How we conceive our physical space depends on our needs. If work is to be done, a ‘productive space’ is necessary. For working as teams and groups, we require ‘communal spaces’ – conference rooms or niches, which also need to have the tools and facilities to aid productivity. Creativity necessitates a different space. Occasionally, a ‘resting space’ may be desired.

Space, often considered as void, does have a quality other than emptiness. Everyone has spatial experiences that express something, however, not always

consciously grasped. We speak of ‘confined feeling’ in a small cave and ‘inspiring’ experience in a temple or church. Spatial experiences are based both on visual cues and the potential for movement. Available light and surrounding colour, texture and decorations are known to influence the experience of space. Spatial experiences both of interiors of buildings and outdoor locations such as gardens, hills, river shores and beaches can be awakened by works of art as well. Humans can distinguish harmony from discord in any spatial relationship.

The seat of emotions, goals and belief systems is considered to be the mental space which has both a cognitive, conscious manual pilot mode and a non-conscious, automatic, emotional, inaccessible intuitive space that functions in the automatic pilot mode. According to the theory of mind, humans have the ability to look at the mental space of another person, have reciprocal resonance in the mind space, interpret and react or decide not to react. The mental space is in continuum with the universal space. Note the difference in one’s feeling when beside a flowing river and when in a noisy environment.

Psychologists of the middle of 19th century initially started the study of how we perceive space. They were concerned with how we recognize an object’s physical appearance or its interactions. Discerning three-dimensional space (cognizing visual space) is considered to be learnt during infancy, using non-conscious inference, and is intimately linked to development of hand–eye coordination.

The neuroscience of spatial cognition integrates theories of neural coding, learning, memory and cognition. Neural codes incorporate spatial information about stimuli and also responses suited to mediate spatial behavior in the immediate environment. Recent studies provide newer understanding of the mechanisms of spatial cognition in mammals, including humans. The hippocampal region in the mammalian brain has detailed representation for spatial awareness. Patients with damaged hippocampi and general episodic amnesia have deficits in spatial orientation and navigation as well. Atrophy in the hippocampal formation is often an early feature in the progression of Alzheimer’s disease. Several space-related phobias are also known and include

claustrophobia (fear of enclosed spaces), agoraphobia (fear of open spaces) and astrophobia (fear of celestial space).

There are evidences to suggest that living organisms may communicate through the medium of space. Apart from language and gesture, communication seems possible by other means such as fragrance, infrasound signals, pheromones, etc. In animal experiments, the mother’s heart rate and blood pressure were found to be abnormal when the offspring were killed under water. Genetically equipped dogs are known to sense epileptic seizures and warn patients early; however, the mechanism is unknown. Animals are also known to recognize early signals of natural disasters. These and para psychological phenomena such as telepathy and clairvoyance could have mechanisms that operate through space, which provides a medium for faster connectivity through vibrations, waves and analogue signals. Other than nerves and hormones, extracellular space could be a medium for connectivity inside animals.

We propose that characteristics of mental and ambient spaces are also determinants of the quality of human health. Studies in this domain must comprise: (i) physicochemical characteristics and molecular interactions within different spatial compartments; (ii) determination of the origin of different forms of energy in various spaces and effects of different types of energy on features in different compartments of space; (iii) relationship of ambient spatial dimensions, forms and energies with homeostasis and complex functions in organisms, and (iv) spatial features that cause disease states.

What is the scope for spatial interventions as a strategy to reverse or modify abnormal cognitive and behavioural functions in humans? Spatial intervention strategies could aim to harmonize resonating frequencies in the body and ambient space, and improve emotional quotient and mental space function. Spatial interventions may aid development and strengthening of the intuitive mind as well as improve emotional resilience and thus possibly reduce professional failures. Recreating past nostalgic space could be effective for rehabilitation of cognitive impairment. Nurturing the intuitive mind space could foster talent in children who are known to have a virgin intuitive space.

Promotion of Cardiovascular Health in the Caribbean Region

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In the month of March, CV Network publishes a report on the annual Caribbean Heart Health Education gala dinner. With the postponement of this event, an article on the incidence of cardiovascular disease (CVD) and diabetes in the Caribbean region is highlighted. It should be mentioned that we have previously published in this subject area of CVD in the Caribbean (D'Oyen et al. 2018. 17(1): 32-36; Rodriguez-Levy and Rodriguez-Portelles. 2018. 17(1): 37-39) as well as Africa (Adeghate. 2018. 17(4): 19-20) regions.

The Caribbean Heart Health Education (CCHHE) Inc. is an organization that was established in 2015. It is mandated to promote the prevention of cardiovascular disease through education in the Caribbean region and the local Winnipeg Caribbean community has been mobilized to assist with this. The objectives of the organization are as follows:

- To involve the Winnipeg Caribbean Community in the promotion of cardiovascular health in the Caribbean countries.
- To promote strategies for prevention of cardiovascular disease in the Caribbean countries.
- To follow the mandate of the International Academy of Cardiovascular Sciences for promoting cardiovascular education, research and prevention.
- To organize symposia, workshops and public forums through the International Academy of Cardiovascular Sciences.
- To develop resources for programming of professional activities.
- To develop a Caribbean section of the International Academy of cardiovascular Sciences.
- To cooperate and collaborate with other Caribbean community organizations in Canada and internationally for promoting cardiovascular health.

I came across a very interesting article entitled: "Improving the Health Status of Caribbean People: Recommendations from the *Triangulating on Health Equity Summit*" appearing in *Global Health Promotion*, volume 21, pages 19-28, 2014¹. This was an excellent read and I will summarize some of the salient features of this article, which I believe are still relevant at this time.

We all know the devastating physical and economic burden of disease at the level of the individual, family, communities, health care delivery and governments. Unfortunately, the impact of socioeconomic and sociocultural factors as determinants of health are all far too evident not only from the global perspective, but even more so in the Caribbean. In the Western hemisphere, the Caribbean region has been most affected by chronic diseases. In fact, the Pan America Health Organization (PAHO) has stated that the Caribbean has the highest death rates from heart disease and the top 5 countries for diabetes in the Americas² and stroke ranks as one of the leading causes of death. The implementation of best practices to improve health outcomes in the Caribbean will require a multifaceted and multidisciplinary approach. However, success will only be achieved if certain barriers and challenges are subsided. These obstacles relate to a) limited research resources, b) policy and governance, c) communication and community engagement, and d) lack of skilled health care personnel.¹

Table showing leading cause of death in the Caribbean, world and high-income countries (adapted from Sastre et al¹)

Cause of death	%		
	Caribbean	World	High income countries
Heart disease	15.7	12.8	15.6
Stroke	10.0	10.8	8.7
Diabetes	10.0	2.2	2.6
Hypertensive diseases	6.0	-	2.3

Important recommendations were put forward at the Best Practices Workgroup session¹ at the above-mentioned summit and are summarized as follows: 1. In view of limited access to health care and health care delivery in some regions of the Caribbean, it was recommended that practitioners need to service patients at the community level sites as transportation for many is a problem. In addition, because of the diverse ethnicities and beliefs in this region, culturally relevant interventions need to be

considered in the development of health care strategies and related to this best practice interventions need to be established by building a trusting environment. 2. The need to involve community members as equal partners in the process of developing, implementing, leading and monitoring health programs. At the same time, practitioners need to determine and understand where community apathy is generated and how awareness and mobilization can be enhanced. 3. It was also recommended that public health and community leaders inform politicians of health issues and understand the consequences if they are not heard. 4. Having a comprehensive approach to health care, and specifically a holistic approach to health that includes social, spiritual, physical, intellectual and environmental health dimensions. 5. In order to improve the health in the Caribbean long-term sustainability is integral to public health in this region. A lasting and effective sustainable

course of action will require mentoring systems, funding, research and education.

You will have noted the objectives of CCHHE, I sincerely believe that this organizations endeavors are consistent with the thoughts of the authors of the article¹. It is hoped that you will understand the severity of the health problems in the Caribbean.

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The Effect of Spaceflight on Heart Cells

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With the turn of the 21st century, space travel has become increasingly common, so much so that some private companies have even floated plans of space tourism. Though space travel is undoubtedly exciting, conditions in the space are strikingly different and can have profound effects on the human body and health. For this reason, astronauts embarking on space travel undergo rigorous physical and mental tests and undertake various protective measures to minimize health risks due to spaceflight. Despite the various precautionary measures, long term spaceflights can cause multiple health problems like bone density loss, loss of muscle mass, adverse effects on cognitive performance, microbial shifts and changes in gene expression. It is therefore essential to understand the effects of spaceflights on human physiology which can help us devise strategies to overcome the limitations [1].

Heart is one of the major organs affected by conditions of microgravity that exists in space. In simple terms, microgravity refers to the condition in space where the effects of gravitational forces are minimal, which causes the people and objects to appear weightless. Microgravity leads to redistribution of body fluids away from the extremities, which can impact cardiovascular physiology. Studies have noted reduced heart rate and lowered arterial pressure under conditions of microgravity. A recent study published in the journal *Science* earlier this year [2], conducted a multi-dimensional analysis of the effect of spaceflight on a pair of twins. The investigators noted that long-term exposure to microgravity reduces mean arterial pressure and increases cardiac output. An article by Wnorowski et al [3], which appeared in the journal *Stem Cell Reports* offers some new insights on the effect of microgravity on cardiac function in humans at cellular and molecular levels. Studies in the past on the effect of microgravity on heart cells have primarily employed rat or mouse-derived cardiomyocytes (heart muscle cells), since it is very difficult to source and propagate human cardiomyocytes. However, Wnorowski and his colleagues employed cardiomyocytes derived from human induced pluripotent stem cells (hiPSCs) generated from mononuclear cells in peripheral blood sourced from three

different individuals. The study therefore offers novel insights into the effect of microgravity on human heart cells in the space.

The scientists grew the cardiomyocytes in specially crafted fully enclosed 6-well plates called Biocells and maintained them in an on-station incubator at the International Space Station. A replicate (an exact copy) plate of cardiomyocytes was maintained at identical conditions at the ground station for comparison. After maintaining the cardiomyocytes for almost 5.5 weeks at the space station, the cardiomyocytes were returned to earth and the structural, functional and molecular properties of the cardiomyocytes were compared with those of the ground controls. Notably, they did not find any marked changes in the overall cellular structure or the cytoskeletal (cell's skeleton structure) organization. Also, the beating rates of the cardiomyocytes were also not significantly different. However, they observed reduced calcium recycling rates in these cardiomyocytes. The calcium flux into and out of the membranous compartments of the cardiomyocytes is critical for their rhythmic beating. In line with this, they observed irregular beating intervals in these cardiomyocytes. This indicates that microgravity can induce changes in the beating pattern even in the isolated heart cells.

Next, to understand the changes at the molecular level, they profiled the changes in the expression levels of the various genes by RNA sequencing. Three distinct samples of cardiomyocytes; a sample of space-flown cardiomyocytes maintained in space for 4.5 weeks, a sample of post-flight cardiomyocytes from day 10 after return from space and a ground control sample at the post-return time point were compared against each other. Though calcium recycling and contractility were impaired in space-flown cardiomyocytes the expression of the genes related to these processes were not significantly altered due to microgravity. This indicates that these defects might be caused due to more direct effects of microgravity on the cellular physiology rather than at the gene-expression level.

Further annotation of the RNA-sequencing data revealed that there was a marked upregulation of the genes related to mitochondrial function in the space-flown cardiomyocytes. On the other hand, genes related to DNA damage and repair and enzymes related to DNA/RNA unpacking were reduced in space-flown cardiomyocytes. Analysis for coordinately regulated set of genes revealed that genes targeted by Sp1 and MEF2 transcription factors were markedly upregulated in the space-flown samples. Finally, analysis of gene expression patterns by two-group comparisons revealed that the number of differentially expressed genes was higher in the space-flown vs ground samples and space-flown vs post-flight samples when compared to ground vs post-flight samples. This suggests that some of the gene-expression changes induced by spaceflight are reversible upon return to normal gravity [4].

The study offers several new insights into the changes caused by spaceflight in cardiomyocytes. However, it is crucial to consider some of the caveats and limitations of the study which the authors also explicitly acknowledge in their article. First of all, in addition to microgravity, the radiation levels are quite high in space which might also have contributed to the observed changes in gene expression.

Next the space-flown samples experienced the additional stress of launch and re-entry, which the ground samples

did not. Finally, the use of hiPSC derived cardiomyocytes poses some limitations. Some fibroblasts were also present in the cardiomyocyte preparations and obtaining a pure population of cardiomyocytes from hiPSC remains a challenge. Though the hiPSC cardiomyocytes represent the best available model, they do not represent the mature cardiac muscle cells in entirety. The study however lays a solid groundwork for future studies in this direction. Technical advancements which can overcome some of the shortcomings noted here can provide a more refined model of the effect of spaceflight on cardiovascular physiology.

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Experience with Vitamin C Intake

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Abstract

The first author undertook a one person study of the effect of increasing the plasma content of vitamin C and its effect on the frequency of infection by common cold, in his own case. The results show that the frequency of catching cold went down remarkably, and there were also some side benefits (reduction of pain in joints and increased energy level).

Introduction

Vitamin C appears to be a very important vitamin for human health (1-6). However, it has also been the subject of controversial conclusions by different research groups,

particularly for specific usefulness, such as cancer treatment (1-6). Du *et al.* (2) conclude that vitamin C is involved in the regulation of over 800 target HIF genes, and is necessary for the functioning of many enzymes responsible for maintaining the biochemical machinery of cells and tissues. An important mechanism of the action of vitamin C is the formation of hydrogen peroxide (H₂O₂) inside human tissue (2), which, in turn, produces other free radicals such as superoxide anion, hydroxyl radicals, and peroxy radicals (7, 8). Simon *et al.* (9) have reviewed the evolution of the immune system in humans, from infancy to old age. The Linus Pauling Institute keeps updating its review of vitamin C (6). To quote from this

review, based on its references 128 and 129, (10 and 11) the following gives some of the positive results: "... a strong inverse relationship [https://lpi.oregonstate.edu/mic/glossary - inverse-association](https://lpi.oregonstate.edu/mic/glossary-inverse-association) between plasma vitamin C and mortality from all-causes, cardiovascular disease, and ischemic heart disease (and cancer in men only) was observed in the EPIC-Norfolk multicenter, prospective cohort study (10). After approximately four years of follow-up in 19,496 men and women (ages 45-79 years), a dose-response relationship was observed such that each 20 $\mu\text{mol/L}$ increase in plasma vitamin C was associated with an estimated 20% risk reduction in all-cause mortality. Similarly, higher serum vitamin C concentrations were associated with decreased risks of cancer-specific and all-cause mortality in 16,008 adults from the US National Health and Nutrition Examination Survey (NHANES) III (1994-1998) (11)". These results, and the conclusion of the review by Simon *et al.* (9) that the immunity level in elders decreases with age, suggests a direct relationship of the human immunity levels with vitamin C levels in human plasma.

Camarena and Wang (3) conclude that vitamin C deficiency of pregnant women could be responsible for birth defect of babies; and that between 10 and 25% of adults in the world may be living with inadequate levels of vitamin C in their plasma. Any usefulness of higher levels of vitamin C in improving human health might contribute to lowering the risk of other health conditions, such as cancer, viral infections, dementia, Parkinson's disease, sepsis, and so on. It should be noted that there are a small number of ailments where high level of vitamin C could be harmful (4).

However, there is a controversy over the use of vitamin C, mainly based upon the following points (1-6): (i) the levels of vitamin C achieved by intravenous injections (IV) are much greater (mM) than the levels achieved by oral administration (<0.2 mM); however, many comparisons for similar investigations have been done by the two different modes of vitamin C administration, without realizing that the two modes lead to different vitamin C concentrations in the blood plasma of the patients; (ii) the toxicity of vitamin C is very low (4) and amounts to little more than the probability of kidney stone formation with large oral doses of vitamin C (>0.5 g/d), though it seems to be acknowledged that this risk only exists in patients with poor kidney function.

Experimental approach

One of us (AS, age 86 y in 2018) has undertaken a one person study of the effect of higher levels of vitamin C in his own blood, on the frequency of the more common infection related to daily life and travel – common cold. Since IV injections of vitamin C on a regular basis are

inconvenient, an alternate method to possibly get the vitamin absorbed directly into the blood has been used (based on the suggestion by a dentist (12)), by placing the capsules containing vitamin C (UTVC; calcium ascorbate, from Natural Factors) under the tongue, and avoiding swallowing the accumulating saliva solution of vitamin C for about 20 minutes (till the crystals of the vitamin seem to have dissolved in the saliva).

Results and Discussion

The initial results in the case of AS have been promising:

- (i) Three days after the start of taking 1 g of vitamin C in the morning (Dec. 12, 2018), AS noticed a reduction of the morning pain in the back, knees and hips, on getting up from the bed. The level of joint pains went down further in two weeks such that the use of Voltaren Emu Gel (GlaxoSmithKline) was reduced from regular, to occasional, applications.
- (ii) AS also noticed an improvement in his energy level. In about a week, this enabled him to walk for one hour at a stretch (~16 min/km), as compared to walking before in stretches of about 30 minutes each, separated by 15-120 minutes. In about 2 weeks, the level of being tired after 1 h walk went down even further. Since then he has been able to walk and play a 9-hole golf course (nominal distance 1.5 km) over one and a half hours, on a daily basis.
- (iii) After about 4 weeks, the UTVC dose was increased from 1 to 2g/d, one in the morning and one in the evening. The dose was further increased to 3 g/d, about 6 weeks later, at which point it is now steady.

Effect on health

- (a) After about a month of starting this experiment, AS travelled to the US for a 2-week trip. He has a tendency to pick up a sinus or throat infection when he travels, about 80% of the time. He completed his trip without an infection.
- (b) About two months after starting UTVC, AS went to India for three weeks. Two days before leaving he came down with a cold, and pain in his eyelids, early in the morning. He took only routine decongestant (a 5-h decongestant (CIPLA; Cetirizine Phenylephrine and Paracetamol)), followed later by one 12-h Eltor tablet (Sanofi). However, on the day the cold started, it seemed to finish by 8 PM the same evening. The eyelid pain had finished by about 1 PM on the same day. Next morning there was no sign of the cold, but another Eltor tablet was taken just to be on the safe-side, because of the trip starting the next day. His health remained very good during the 3 weeks in India, even with over a dozen mosquito bites (despite all the precautions), and since return from India. This was the first time AS has had a one day

cold. Usually his colds last at least 5 days and are generally followed by a persistent cough.

- (c) About April 23rd, AS developed a bacterial infection in his right foot. It cleared with a 5-day course of anti-biotics.
- (d) From May 1st to May 5th, AS visited Manitoba, without any health problem.
- (e) In 2nd week of August: AS visited Manitoba, Connecticut and New York for 2 weeks, without any health problem.
- (f) In 2nd week of September: AS visited Chicago and Winnipeg for 10 days, without any health problem.

The levels of vitamin C in AS blood have been measured (LifeLabs in Victoria, BC, Canada (13)) with the following results (supplemental vitamin C dose till Dec. 11: 500 mg/d)

Date	Vitamin C level (µmol/L)	dose, g/d (UTCV)
2018:		
Dec. 12	48	0.5
Dec. 28	80	1.0
2019:		
Mar. 20	97	2.0 (from Dec. 31)
April 26	132	3.0 (from Mar. 30)
May 28	77	0.5 to 3.0
July 02	98	3.0 (from May 24)
Aug. 03	119	3.0
Sept. 16	154	3.0
Oct. 29	119	3.0
Nov. 21	171	0 to 3.0
Dec. 16	154	3.0 (from Nov. 18)
2020:		
Jan. 23	138	3.0

Since Dec. 12th, 2018, AS has enjoyed much better health than at any time in the last 5 years.

Concluding remarks

Given that this study was of one person only, not blinded; so the placebo effect cannot be ruled out. Nevertheless, this one person study indicates that increasing the level of vitamin C in one's blood plasma may improve general health, and reduce the frequency of infection (cold)

sustained in daily life, and as a result of travel by air. It is hoped that the medical community might evaluate this result and consider pursuing this approach with a properly designed study of the potential prevention of adverse health conditions by vitamin C, which, in turn, may lead to overall better human health at lower costs. Since there is some evidence (1-6) to support some level of protection by vitamin C against viral infections, it may also be worth trying its effectiveness against Chikungunya, Dengue, Ebola, West Nile, and Zika, as well as potential other new viral infections. From this point of view, two earlier drafts of this paper have been sent to World Health Organization (Jan./Feb., 2020).

Camarena and Wang (3) have also pointed to the likelihood of birth defects in babies due to low vitamin levels in the plasma of their mothers, during pregnancy. Optimization of plasma vitamin C levels in pregnant women for reduced birth defects of their babies may be worth investigation. Early availability of needleless injection devices (14) may also be useful in many cases. The increased convenience of vitamin C injections administered routinely by the patients themselves, may contribute to improved human health.

Acknowledgements

AS thanks Dr. Roger Howell for bringing up his work on radioprotection by vitamin C (15), during a leisurely discussion over a lunch in September 2018, in which he touched on the instability of vitamin C on exposure to air. Since AS had also done some work in this area (16), his interest in this topic led him to investigate this instability in the following months by the study of some of the vast amount of therapeutic, but controversial, work on vitamin C, which then led to the work presented in this paper. AS is grateful to Dr. A. David Attwell to encourage this effort, and provide needed guidance during this work. The authors thank Dr. Brian Lentle for helpful comments on an earlier version of this manuscript.

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An Overview of Insight on Hypertension in Jordan

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Cardiovascular diseases (CVDs) represent a major health issue and is a leading cause of morbidity and mortality worldwide. Hypertension is one of the resilient modifiable risk factors for CVDs and is a high burden on the healthcare systems globally due to the high prevalence and related mortality and morbidity[1]. The intimate relationship between blood pressure and CVDs makes the distinction between high normal blood pressure and hypertension based on random cut-off values for blood pressures[2]. The prevalence values of hypertension in the general population of Europe and United States were reported to be 30-45% and 29-40%, respectively, with a sharp increase with age [3, 4]. It has been reported that the prevalence of hypertension is on the rise, as well as death due to related hypertension complications [1, 2, 5, 6].

In adult Arab population, hypertension was reported to be approximately 30%[7]. A substantial increase in the prevalence of hypertension in Jordan, from 29.4% to 32.3% during the period 1994 to 2009 was noted[8]. The limitations in preventive actions such as early detection as

well as hypertension control caused an increased risk of cardiovascular events in Jordan. Additionally, population based studies as well as hypertension prevention and awareness programs are crucial for lowering cardiovascular events such as myocardial infarction due to hypertensive disease in the country.

A recent study reported that approximately one-third of adult population in Jordan are suffering from hypertensive disorder with a higher prevalence in men than in women, 33.8 and 29.4%, respectively[9]. While hypertension prevalence among Arabs was reported to vary, ranging from 26 to 29.5%[5, 7], such differences in the range of the disease could be due to variations in experimental study design methods and procedures. Furthermore, this higher prevalence of hypertensive disease among Jordanians and other Arab populations could be due to increased obesity, sedentary life style, and increased consumption of fast, fatty and salty food[10].

The prevalence of hypertension in both sexes is age-dependent as it increases with ageing, which was reported among many ethnic populations including Arabs[8, 11–13].

There is no agreement on the gender prevalence of hypertension in Arabs. While some studies reported higher rates of hypertension in men than in women [11, 14, 15], some reported the opposite[16–18], while others reported no gender significance[19, 20].

The reported awareness of hypertension in Arabs widely varied, ranging from 18% to 79.8% [7] A study on Jordanian population, reported that 57.7% of males and 62.5% of females were aware of having hypertensive disorder [9]. Globally, awareness of hypertension ranged from 25% to 75% and among developed population, 50% to 75% of patients were aware of having hypertension [5]. Khader and coworkers reported that the awareness among Jordanians has increased substantially in recent years, they showed a rate increase from 39.8% to 57.7% in men and from 51.8% to 62.5% in women in the years 2009 and 2017, respectively[9]. This increase in awareness is undoubtedly due to recent improvements and expansions in healthcare services in Jordan.

The rate of hypertension control varied significantly worldwide[12], in Arab countries, however it ranged from 8% to 44% [11, 14–19]. Reports show that nearly 33% of Jordanian patients being treated with antihypertensive agents have controlled hypertension. Even though, with recent enhancement and expansion of healthcare services in Jordan, control of hypertension is still unsatisfactory, which could be due to poor management and patient's noncompliance. Nonetheless, improvement in the control of hypertension has been seen recently, it increased from 17.4% to 30.7% in males and from 18.6% to 30.7% in females in the years 2009 and 2017, respectively. Such improvement in hypertension control is probably due to patients better awareness and recent enhancements to the provided healthcare services[9].

Recently, Khader and coworkers have shown that patients over 50 years old have a greater chance of developing hypertension and have better awareness and controlled hypertension more than younger ones. Usually, due to other comorbidities, older patients more frequently seek and access healthcare services than younger ones, thus resulted in higher awareness and control of their hypertension. Additionally, those with family history of hypertension are more likely to be aware of the disease and seek healthcare help and treatment if hypertensive.

Metabolic syndrome, which increases the risk of cardiovascular diseases, is a cluster of conditions including diabetes mellitus, increased waist

circumference, and abnormal cholesterol or triglyceride levels. Such conditions are closely linked to hypertension. While 33% of adult Jordan population are suffering from hypertension, 50% of those are aware of having the disease and only 33% of those are having controlled hypertension with medications. This level of uncontrolled hypertension is still unacceptable and could be explained by poor hypertension management in Jordan. Healthcare providers should establish better measures to increase public awareness of hypertension and promote healthier lifestyle.

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Dr. Mohamad Nusier



*Dr. Mohamad
Nusier*

Professional Achievements:

Mohamad Nusier is a Professor of Biochemistry and Molecular Biology at Jordan University of Science and Technology, School of Medicine (JUST). Dr. Nusier received his MD in 1986 from Kyiv Medical University in Former Soviet Union and his PhD in 1996 from the Bowman Gray School of Medicine at Wake Forest University, NC, USA. He did his postdoctoral training at Smith Kline Beecham

Pharmaceuticals, Collegeville PA, USA. He joined the Medical School at JUST as an assistant professor, and he was promoted to an associate professor in 2004 and to a full professor in 2009. During that period, he served as a chair for the Department of Biochemistry and Molecular Biology. From 2009-2011 he served as a medical director for Medlabs Medical Laboratories in Kuwait, where he managed Royale Hayat Hospital Laboratories. Two years later, he joined United Laboratories in Kuwait, where he headed Al-Seef Hospital Laboratories and the Medical Genetics Laboratories, including the Newborn Screening Program.

In 2013, he returned to JUST as a professor and was asked to join a team to establish a new medical school, where he served as Vice President for Academic Affairs and Dean of Research for the Royal University for Medical Sciences in Amman, Jordan. He received Jordan Ministry of Higher Education Scholarship to the Medical School and Jordan University of Science and Technology Scholarship to Wake Forest University School of Medicine. Abdel Hamid Shouman Association, Jordan

acknowledged him as a distinguished professor. He also served as a consultant for the WHO and Ministry of Environment of Jordan on the adverse effect of Lead on health, a project aimed to phase out Lead from gasoline in Jordan in 2006.

He is on the editorial board and a reviewer for several biomedical and medical Journals and a member of the Jordanian Lipid and Hypertension Society. Dr. Nusier served as an advisor, a committee member and external examiner for over 30 graduate students. He also received several national and international grants and collaborated with many scientists and researchers from the US, Canada and Europe, attended and spoke at many national and international conferences. Dr. Nusier research interest is genetic mapping of collagen disorders such as Papillon-Lefèvre syndrome, prepubertal periodontitis and amelogenesis imperfecta.

Genetic variations of type 2 diabetes mellitus (T2DM) and it is link to heart diseases:

Dr. Nusier was PI of a Jordanian group who participated in the diabetes heart study in collaboration with Wake Forest University. Over 1200 samples for clinical biochemical and mutational studies were collected from a single large Jordanian family known to have high prevalence of DM and cardiovascular diseases (CVD). It worth noting that customary consanguineous marriages in such families, made them excellent candidates for constructing pedigrees and genetic linkage and mapping studies. With the data accumulated in this family study, they conduct heritability and familial aggregation analyses on the measures of T2DM. Primary phenotypic



measures include T2DM, cardiovascular disease (CVD), and renal function. Such analyses were used to characterize the relative contribution of genetic and environmental factors to T2DM and CVD, and results were used to guide subsequent genetic analysis. An epidemiologic exploration approach was used to determine cardiovascular disease as it pertains to individuals with Type 2 diabetes.

Currently, Dr. Nusier is spending a year of his sabbatical leave as Visiting Professor at the Institute of Cardiovascular Sciences, St. Boniface Hospital Albrechtsen Research Centre in Winnipeg. He is engaged in scientific deliberations with Dr. Naranjan S. Dhalla on subcellular defects in Ca²⁺-handling in cardiovascular disease.

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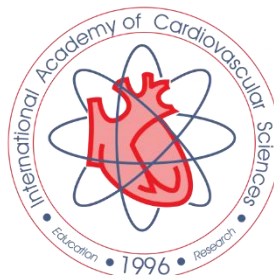
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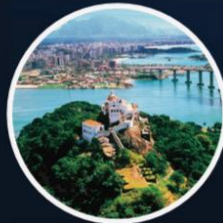


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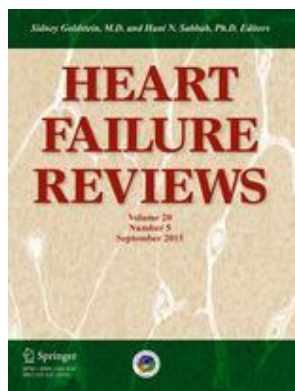
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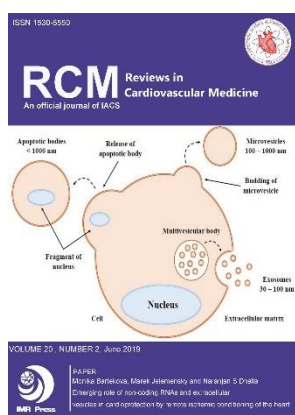
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