



**DANONE
NUTRICIA**
RESEARCH



LUNCHEON SYMPOSIUM
WORLD CONGRESS OF NEPHROLOGY 2017

Advancements in the effects of hydration in kidney health

*Avances en los efectos de la hidratación
en la salud renal*



Sunday, April 23rd • 13:15 - 14:30 • Valparaiso 1 • MEXICO CITY



Chair / Presidente **Richard J. Johnson, M.D.**, University of Colorado, USA

💧 **Cross-talk mechanisms between fructokinase and vasopressin/copeptin in chronic recurrent dehydration and kidney disease**

Mecanismos de interferencia entre la fructoquinasa y la vasopresina/copeptina en la deshidratación crónica recurrente y la enfermedad renal

Laura G. Sánchez-Lozada, Ph.D., INC Ignacio Chávez, Mexico

Introduction of the Hydration for Kidney Health Initiative / Introducción de la iniciativa de la hidratación en la salud renal by **Louise Moist, M.D., M.Sc.**, Western University, London, Canada

💧 **Plasma copeptin as a predictor of cardiorenal disease – population based prospective cohort studies and a mendelian randomization approach**

Plasma copeptina como predictor de la enfermedad cardiorenal – Estudios prospectivos de cohorte basados en la población y un enfoque aleatorio mendeliano

Sofia Enhörning, M.D., Ph.D., Skåne University Hospital, Lund University, Sweden

💧 **Expanding our knowledge: Hydration for Kidney Health Initiative second call for research**

Ampliando nuestros conocimientos: Iniciativa de la hidratación en la salud renal segunda convocatoria de propuestas de investigación

Louise Moist, M.D., M.Sc., Western University, London, Canada

CHAIRMAN OF THE SESSION, **Richard J. Johnson, M.D.**

Professor, School of Medicine, Renal Diseases and Hypertension, University of Colorado



Prof. Richard Johnson is a Professor and Chief of the Division of Renal Diseases and Hypertension at the University of Colorado, in Denver, USA. He is associate Director of the Colorado Obesity Research Initiative. Since graduating and gaining Fellowships in Nephrology and Infectious Disease from the University of Washington, in Seattle. Prof. Johnson focused his research on the pathogenesis of kidney diseases, with special interest in the role of chronic dehydration in kidney disease. Prof. Johnson's recent research examined the role of subtle renal injury in salt sensitive hypertension and uric acid and fructose in

the pathogenesis of hypertension, metabolic syndrome, and diabetic kidney disease. This research work revealed that raising uric acid could be a risk factor in kidney disease. This research work revealed that raising uric acid could be a risk factor in kidney disease as a result of inducing inflammatory and pro-oxidative effects in vascular cells. Prof. Johnson is a prolific author with over 500 publications and a number of books in the field of nephrology. Prof. Johnson has served on the International Society of Nephrology (ISN) Executive Committee and has been an ISN Councilor for the United State. In 2011 he was the ISN Scientific Program Chairman for Vancouver ISN. Prof. Richard Johnson also received the New Inventor of the Year Award from the University of Colorado Medical Campus, Denver in 2011.

Laura G. Sánchez-Lozada, Ph.D.

Renal Pathophysiology Laboratory, INC Ignacio Chávez, Mexico



Dr. Laura Gabriela Sánchez-Lozada is a research scientist in the Laboratory of Renal Physiopathology at the Instituto Nacional de Cardiología “Ignacio Chavez” in Mexico City. She graduated in the National Autonomous University of Mexico with a major in Biology, and obtained her Ph.D. degree in Biomedical Research in the National Polytechnic Institute. Her research interest has focused on uric acid and hyperuricemia as a causal factor for hypertension and renal disease, and also on the role of sugar, especially fructose, in driving obesity, diabetes, kidney damage and hypertension.

Currently she is investigating the role of hydration on kidney disease, focusing on the possible participation of sweetened beverages in exacerbating kidney injury. Her work includes studies ranging experimental renal physiology, cell culture, mitochondrial function, and human studies as well. Her research has been funded by the National Council of Science and Technology (CONACyT, Mexico), National Institutes of Health (USA) and pharmaceutical industry. Dr. Sanchez-Lozada is recognized as a Level III National Researcher by the National System of Researchers –CONACyT (Mexico).

CROSS-TALK MECHANISMS BETWEEN FRUCTOKINASE AND VASOPRESSIN / COPEPTIN IN CHRONIC RECURRENT DEHYDRATION AND KIDNEY DISEASE

There is increasing evidence showing a trend towards a decrement in the ingestion of tap water and its substitution with sweetened beverages as a mean to provide hydration fluids. Epidemiological studies have demonstrated that a chronic suboptimal consumption of water is associated with the development of chronic kidney disease. Moreover, epidemics of chronic kidney disease of unknown cause has been described in agricultural communities located in tropical geographical areas. The disease in Central America has been named Mesoamerican Nephropathy and presents with an asymptomatic elevation of serum creatinine, mild proteinuria and an important component of tubulointerstitial damage. In this disease, the strongest epidemiological risk factor appears to be repetitive episodes of dehydration. Experimental studies have shown that recurrent dehydration and heat stress activate vasopressin and polyol-fructokinase pathways which cause chronic kidney damage. The injury is exacerbated by rehydration with fructose-containing beverages by further overactivation such pathways. Thus, rehydration with even small amounts of fructose can induce impaired renal function and tubular injury associated with oxidative stress, systemic inflammation, and mitochondrial dysfunction. The mechanism by which fructose causes renal injury is by stimulating vasopressin, and blocking vasopressin receptors largely protects against the renal injury. Thus, there is a major crosstalk between vasopressin and fructose metabolism. These studies highlight the importance of the type of fluids used as rehydration and also on growing recognition of the interaction of fructose and vasopressin in disease.

Sofia Enhörning, M.D., Ph.D.

Internal Medicine, Department of Clinical Sciences, Skåne University Hospital, Lund University, Malmö, Sweden



Dr. Sofia Enhörning is a post-doctoral researcher at the department of Clinical Sciences at Lund University and a medical doctor at the department of Endocrinology at Skane University Hospital in Lund, Sweden. She graduated from medical school at Lund University and obtained her Ph.D. degree in Internal Medicine at Lund University. Her research has focused on genetical and epidemiological studies of the vasopressin system and its links to metabolic disease. She is currently focusing on experimental intervention studies, investigating the role of hydration on the vasopressin system and gluco-regulatory hormones, and on epidemiological studies, investigating the links between the vasopressin marker copeptin and renal disease. Furthermore, she is investigating genetic predisposition for altered copeptin levels and will use a Mendelian Randomization approach to study if elevated copeptin is causally related with renal and cardiometabolic disease. Dr. Enhörning has received the Scandinavian Society for the Study of Diabetes (SSSD) Young Investigation Award and the "best clinical diabetes thesis of the year" award in 2012 from the Swedish Society for Diabetology. In 2016, she was awarded with the Hydration and Kidney Health Grant.

PLASMA COPEPTIN AS A PREDICTOR OF CARDIORENAL DISEASE – POPULATION BASED PROSPECTIVE COHORT STUDIES AND A MENDELIAN RANDOMIZATION APPROACH

Vasopressin (VP), also known as antidiuretic hormone, is a vasopressor and antidiuretic peptide commonly known as an important operator in the salt and water regulation of the body. We and other groups recently established a link between the VP system and several cardiometabolic risk factors. Elevated VP, measured as copeptin (the C-terminal cleavage product of the VP precursor), predicts development of type 2 diabetes and abdominal obesity, and is an independent risk factor for diabetic heart disease and premature mortality. We are currently investigating effects of increased hydration on copeptin, glycemia and gluco-regulatory hormones.

Previous studies in humans and animals suggest a role for VP in renal function decline both in diabetes patients and in the general population. We are currently studying the link between copeptin and incident renal disease in large population based cohorts including the Malmö Diet and Cancer - Cardiovascular Cohort (n=5300) and the Malmö Preventive Project (n=5400). Copeptin is measured at baseline in the populations and disease is captured using nation-wide registers. Furthermore, we are planning a Mendelian Randomization study to test if VP (measured as copeptin) is causally related with renal and cardiometabolic disease. Susceptibility genes associated with altered copeptin levels will be identified using data from genome-wide association studies conducted in the Malmö Diet and Cancer - Cardiovascular Cohort, the Malmö Preventive Project, the FINRISK-97 cohort and the PREVEND cohort, followed by test of association with metabolic and cardiorenal disease in the DIAGRAM and CARDIOGRAM cohorts.

Our previous and current data suggest that copeptin is an independent predictor of cardiometabolic and renal diseases which can be used to identify individuals that are at higher risk for developing diabetes, renal disease and its cardiovascular complications in order to offer early preventive strategies.

Louise Moist, M.D., M.Sc.

Professor of Medicine, Epidemiology and Biostatistics

Scientist, Program of Experimental Medicine

Deputy Chair Division of Nephrology, Western University, London, Canada



Dr. Louise Moist is a Nephrologist, Professor of Medicine and Epidemiology and Biostatistics, Associate Chair of the Division of Nephrology and Scientist in the Program of Experimental Medicine at Western University, London, Canada. Her clinical and research interests are focused on: the prevention of chronic kidney disease, with a special interest in hydration; and dialysis, with expertise in the vascular access for hemodialysis. Dr. Moist has a number of leadership roles including The Ontario Renal Network Physician Lead for Dialysis Access, the Internal Medicine Physician Lead for the SW

Local Health Integrated Network, and Chair of the ISN-H4KH Research Initiative. Dr. Moist is a recognized educator, clinician and researcher with multiple achievement awards, research grants and over 130 peer reviewed academic papers.

INTRODUCTION OF THE HYDRATION FOR KIDNEY HEALTH INITIATIVE

EXPANDING OUR KNOWLEDGE: HYDRATION FOR KIDNEY HEALTH INITIATIVE SECOND CALL FOR RESEARCH



Danone Nutricia Research and the ISN have collaborated to create **the HYDRATION for KIDNEY HEALTH (H4KH)** Research Initiative to stimulate interest of both established and new researchers to explore the role of hydration in kidney health. This need for science and evidence is driven by the recognition of detrimental effects of dehydration, heat and environmental factors on kidney function.

The objectives of the **H4KH** Research Initiative are to: enhance awareness and level of scientific evidence of the effects of hydration on kidney health; expand research capacity by supporting investigators focusing on prevention of chronic kidney disease; engage researchers in the development of trans-disciplinary research networks and to create sustainable momentum in supporting research in this field of study.

Three research opportunities have been created to meet the above objectives. They include: The ISN-H4KH New Investigator Award, the H4KH Research Grant and the inaugural H4KH Fellowship Grant.

The ISN-H4KH New Investigator Award is available to researchers, within the first five years of their first faculty appointment, who have a M.D. and/or PhD. The awardee will spend 6-12 month training in an international nephrology research center to develop the research skills and capacity to sustain research in H4KH in their academic environment. The first awardee in 2015, was Dr. Fabiana Nerbass, from Fundação Pró-Rim, Joinville, Brazil who is investigating the “Kidney health in Brazilian industrial workers exposed to heat stress and dehydration”.

The ISN-H4KH Hydration and Kidney Health Grant is available to researchers with expertise in and access to: reliable and valid data in an existing data base, data reflective of a representative sample of the general population and or a population with chronic kidney disease (CKD). The 2015 ISN-H4KH Hydration and Kidney Health Grant was awarded to Dr. Sofia Enhörning, from Skåne University Hospital, Malmö, Sweden who is studying “Plasma copeptin as a predictor of, and copeptin associated loci in, cardiorenal disease – population based prospective cohort studies and a mendelian randomization approach”.

The inaugural, ISN H4KH Research Fellowship is intended to stimulate interest of both established and new researchers to explore the role of hydration in kidney health. The applicant will spend 12 months of the year at Danone Nutricia Research, in Palaiseau (Paris) in France to learn and integrate the science on hydration and hydration biomarkers. The applicant would gain exposure and skills both in epidemiology and intervention studies. The grant will be introduced at the WCN Mexico in April 2017.



ISN
H4KH
INITIATIVE

Hydration for Kidney Health [H4KH] Research Initiative

Danone Nutricia Research and the ISN have collaborated to create the HYDRATION for KIDNEY HEALTH Research Initiative to explore the role of hydration in kidney health.

Candidates from all disciplines relevant to kidney disease (clinical, health services and population health disciplines) can apply.

Application
deadline
October 1st,
2017

Explore the role
of hydration in
kidney health with
a research grant

TO APPLY
OR FIND OUT MORE:
WWW.THEISN.ORG/H4KH

NEW



ISN
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INITIATIVE

ISN-H4KH FELLOWSHIP IN HYDRATION FOR KIDNEY HEALTH

Danone Nutricia Research and the ISN have collaborated to create the **ISN-H4KH Fellowship in Hydration for Kidney Health** to stimulate interest of both established and new researchers to explore the role of hydration in kidney health.

The objectives of the ISN-H4KH Fellowship in Hydration for Kidney Health:

- ◆ To enhance awareness and knowledge on hydration and hydration biomarkers
- ◆ To expand the level of scientific evidence on the effects of hydration on kidney health
- ◆ To engage researchers in the development of transdisciplinary research networks
- ◆ To create sustainable momentum in supporting research in the effect of hydration and kidney health

Application deadline
May 1st, 2017
www.theisn.org/h4kh





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