The warmest of welcomes to Wonderful Copenhagen for the 55th ERA-EDTA Congress – that was the message to delegates at yesterday's Grand Opening Ceremony from Bo Feldt-Rasmussen, Congress President, Ulla Wewer, Dean of Health and Medical Sciences, University of Copenhagen, Carmine Zoccali, ERA-EDTA President, and Lisbet Brandi, President of the Danish Society of Nephrology.

Since the ERA-EDTA Congress was last held in Copenhagen in 2002, there have been many changes within nephrology. This new environment comes to life in the theme of the Congress: "Kidney disease – new paradigms, new challenges. New challenges, new opportunities". Nephrology's proud record in meeting challenges and opportunities of scientific research and clinical practice is epitomized by the four awards presented at the Grand Opening Ceremony for outstanding contributions and achievement. The recipient of the 2018 ERA-EDTA Award for Outstanding Clinical Contributions to Nephrology is Professor Jürgen Floege, head of the Division of Nephrology and Immunology at the University of Aachen, Germany. He has been responsible for many scientific achievements and has contributed to major trials in glomerular disease and CKD-MBD, including as creator and leader of the investigator-initiated STOP-IgAN trial. The 2018 ERA-EDTA Award for Outstanding Basic Science Contributions to Nephrology was presented to Professor Hans-Joachim Anders, who is currently Head of the Renal Division at the Inner City Campus, University of Munich. Professor Anders is a physician-scientist whose research focuses on translational aspects of kidney disease. Professor Andrzej Więcek was presented with the Award for Outstanding Contributions to ERA-EDTA. Since joining the ERA-EDTA 30 years ago, he has been a member of the Council, Secretary-Treasurer, and President (2014 – 17). He has been responsible for many innovative activities, including CME courses and the Young Nephrologists' Platform. Last, but not least, the Stanley Shaldon Award for Young Investigators was presented to Dr Shrikant Ramesh Mulay, Assistant Professor at Ludwig Maximilians University of Munich Faculty of Medicine, Medical Clinic and Policlinic IV. He leads the research group aiming to understand complex renal pathologies. The Ceremony closed on a high note with a fascinating plenary lecture from Professor Toni Cathomen (Freiburg, Germany) on "Gene editing: powerful new tool for nephrology research and therapy".

SHINE THE LIGHT ON NEW WAYS OF TREATING YOUR PATIENTS
Come discover new renal care possibilities
VISIT US AT → BOOTH 3.161

SAVING AND SUSTAINING LIVES

 cabrera
The warmest of welcomes to Wonderful Copenhagen for the 55th ERA-EDTA Congress – that was the message to delegates at yesterday's Grand Opening Ceremony from Bo Feldt-Rasmussen, Congress President, Ulla Wewer, Dean of Health and Medical Sciences, University of Copenhagen, Carmine Zoccali, ERA-EDTA President, and Lisbet Brandi, President of the Danish Society of Nephrology.

Since the ERA-EDTA Congress was last held in Copenhagen in 2002, there have been many changes within nephrology. This new environment comes to life in the theme of the Congress: "Kidney disease – new paradigms, new challenges. New challenges, new opportunities". Nephrology's proud record in meeting challenges and opportunities of scientific research and clinical practice is epitomized by the four awards presented at the Grand Opening Ceremony for outstanding contributions and achievement. The recipient of the 2018 ERA-EDTA Award for Outstanding Basic Science Contributions to Nephrology was presented to Professor Hans-Joachim Anders, who is currently Head of the Renal Division at the Inner City Campus, University of Munich. Professor Anders is a physician-scientist whose research focuses on translational aspects of kidney disease. Professor Andrzej Więcek was presented with the Award for Outstanding Contributions to ERA-EDTA. Since joining the ERA-EDTA 30 years ago, he has been a member of the Council, Secretary-Treasurer, and President (2014–17). He has been responsible for many innovative activities, including CME courses and the Young Nephrologists' Platform. Last, but not least, the Stanley Shaldon Award for Young Investigators was presented to Dr Shrikant Ramesh Mulay, Assistant Professor at Ludwig Maximilians University of Medicine, Medical Clinic and Polyclinic IV. He leads the research group aiming to understand complex renal pathologies. The Ceremony closed on a high note with a fascinating plenary lecture from Professor Toni Cathomen (Freiburg, Germany) on "Gene editing: powerful new tool for nephrology research and therapy."
You have been President of the ERA-EDTA for one year now — are you happy with how the association has developed during that time? I have had the privilege to serve the ERA-EDTA in the role of Chairman of the Registry, Editor in Chief of ‘Nephrology, Dialysis and Transplantation’ and now as President of the Society. So I have in-depth knowledge of the strong and weak points of the ERA-EDTA. I believe our society has enjoyed solid growth over the past 20 years and that the many activities it has undertaken need to be better organized into a framework aimed at maximizing internal and external collaboration. This is of obvious importance in a scenario where competition for health research resources and for delivering educational activities are on the rise both within and outside nephrology.

When I was interviewed last year, I said that the society would have to be reorganized into a Clinical Governance branch and a Renal Research branch and that educational and research activities would have to be reformed. Over the past year, the Council has worked intensively and successfully on these proposals, and we have already started to implement this plan. The Council elected a Clinical Governance chair (Professor Ziad Massy) and a Renal Research chair (Professor Dario Filippi). The restructuring of the activities of our Society will be completed next year during the Budapest Congress, where a new type of Continuous Education and Professional Development (CEPD) course will be launched. We also intend to organize WEB-based CME courses, and a very good one on Critical Appraisal in Nephrology will be available very soon. We aim to facilitate the formation of consortia among European nephrologists in order to channel large-scale projects focusing on renal science to the European Commission. I am quite satisfied about our achievements and hope that ERA-EDTA members will take advantage of the efforts being made by the Council to enlarge and improve the educational proposals and research opportunities that the ERA-EDTA will offer.

What milestones have been reached? As already discussed in response to your first question, the reorganization has now been formalized and approved by the Council, and we have elected two new chairpersons who will overlook clinical governance and renal science activities. The redesigned educational courses will have a new focus. Whereas in the past, the pre-congress courses run by the Working Groups presented diverse issues including basic science novelties, new hypotheses and clinical advancements, the new courses will focus primarily on updating the clinical nephrologist on advancements in renal science that may impact upon clinical practice. These courses will be specifically linked to career concerns, which is now demanded in most countries for the certification of updating activities.

What are your current goals for the society? Is there anything special you would like to be associated with, let’s say, ten years — e.g. as the “ERA-EDTA president who did/did not initiate/reorganized/…”? I firmly believe that achievements of scientific societies like the ERA-EDTA are never the result of the efforts of a single person. In serving the society in the present and in past roles, I have made a major effort to create a shared interest environment. I have worked carefully and frankly discussed. In such an environment, the contribution of any single individual is always diluted, and the development of ideas, projects and plans truly results from the contribution of many. I believe that I introduced several innovations in the past, from the creation of NDT Educational to the redesign and the growth of NDT, promotion of the educational activities of the ERA-EDTA Registry and now the restructuring of the activities of our society. I would feel gratified if my name would be associated with the drive to innovate the ERA-EDTA and with my efforts to create an “intellectual chemistry” that facilitates innovation.

Let’s discuss the issue of recruiting young nephrologists. How can nephrology attract more medical students in the future? Let’s make one point clear. The recruitment of nephrologists is not a priority in every country today. In Italy, my own country, the number of nephrologists per million population is about 50, which is among the highest worldwide. So in that country, the problem faced today is that of attracting the best medical students to nephrology and optimizing the use of the present renal workforce, rather than expanding recruiting. Facilitating recruitment and attracting the best young doctors are very different problems that demand the deployment of different strategies. In brief, to attract the brightest medical students to nephrology, one can envisage establishing early contact in order to expose them to the fascinating attractions of nephrology, the specialty which encompasses multisystem pathologies and that offers excellent opportunities for bench to bedside research. The type of contacts I alude to should be the ones loved by the young generations, i.e. WEB based and interactive. In this respect we plan to build a special platform dedicated to medical students and with that aim in mind we will ask the national societies of nephrology for help in designing the platform’s profile to meet the needs of the individual country. This is not an easy task, requiring time-consuming, but we are resolute in pursuing the goal of exposing young medical students to the fascinating discipline of nephrology. In other countries, like the USA, there are vacancies in nephrology training programs and, sadly so, in other several countries there is no funding to establish training programs. In the first case, injecting cultural stimuli is just one aspect of the problem and most probably not the major one. When training programs in a given specialty remain unfilled, the most frequent reason is very pro-saic. In the USA, the insufficient number of trainees in nephrology is due, at least in part, to the fact that nephrologists are economically less rewarded as compared to other specialists or because other specialties create better opportunities for career advancement and life prospects. In such a case, it is essential to lobby for the creation of incentives for nephrologists. In economically underdeveloped countries, nephrology leaders should strive to ensure that the resources devoted to combating renal diseases reach national level and are proportional to the health burden of kidney diseases, which is a tantalizing undertaking.

The support of young nephrologists is on the agenda of the ERA-EDTA. What exactly can the ERA-EDTA do for young nephrologists — and what can young nephrologists do for the ERA-EDTA? The ERA-EDTA is virtually unmarked by any other scientific society with regard to activities aimed at involving nephrologists in the early years of their career. My predecessor, Professor Andrzej Więcek, created the Young Nephrology Platform, an initiative aimed at stimulating the participation of young nephrologists in the life of our society and at giving visibility to the best young investigators. The Council has decided to expand this initiative further. This year in Copenhagen, we substantively increased the number of young nephrologists invited to lecture or present abstracts in the symposia of the main Congress. Furthermore, the Council prioritizes the involvement of young nephrologists in symposia co-organized with other societies whenever possible. We will do our best to promote the active participation of young nephrologists within the boards of working groups. Members of the Young Nephrology Platform are already successfully involved on the Board of NDT.

Apart from the current and future shortage of nephrologists in some countries — what are the challenges European nephrology faces these days? The first problem is the economic sustainability of renal care. About 3% to 5% of health expenditure in most European countries and in the USA are absorbed by patients on dialysis. These patients represent just a tiny fraction (0.1% – 0.2%) of the general population. This may become a problem in a scenario where there is an ascending health burden by severer and severer chronic diseases, which is a tantalizing undertaking. For example, gene therapy is currently being tested only for diseases that have no other cures. However, this is a rapidly growing area and in 10 or 20 years genes will be increasingly used to treat or prevent various diseases. In the future, gene therapists may apply their expertise to treat problems in various different fields, including oncology, cardiology, nephrology, transplantation, etc., thus creating interventional opportunities that cut across today’s specialties. Specialization, which has granted higher quality medicine over the past century, is now perceived as being less than ideal for granting continuity of care. In the present context dominated by chronic diseases, efforts are being made at reducing the trend to overspecialization and at creating flexibility within the health workforce. The health workforce is being profoundly restructured. Doctors are and will increasingly be flanked by new kinds of health professional: medical assistants, health managers, information scientists and others. The restructuring of the renal workforce has already started in many countries, and this restructuring will determine a decrease rather than an increase of nephrologists.

In brief, like other major medical specialties, nephrology faces tantalizing challenges in today’s rapidly changing health scenario. Nephrology should face these problems frankly and make every effort to increase awareness of the same problems within the renal community. Transparent discussion of these issues is the best way to prepare nephrologists for changes occurring in the short to medium term (10–20 years or so) and to transform challenges into opportunities.

You pointed out that interdisciplinarity is a key to strengthening nephrology. Is this the reason why you actively collaborate with neighboring disciplines? I elaborated on the risks of overspecialization when answering the previous question. I firmly believe that collaboration with other specialties is fundamental today and will increasingly be so in the future. What is real collaboration among specialties? It means creating occasions for openly discussing shared problems. In such a case, the territory of general practitioners will be specifically linked to credit-hours, which is an aspect that equally concerns the territory of general practitioners and the renal field. These territorial stimuli is just one aspect of the problem. In economically underdeveloped countries, nephrology leaders should strive to ensure that the resources devoted to combating renal diseases reach national level and are proportional to the health burden of kidney diseases, which is a tantalizing undertaking. In economically underdeveloped countries, nephrology leaders should strive to ensure that the resources devoted to combating renal diseases reach national level and are proportional to the health burden of kidney diseases, which is a tantalizing undertaking.
es intellectual cross-fertilization, i.e. when different specialists leave the room with clearer ideas, new stimuli and new proposals for intensified collaboration with other colleagues both in patient care and in scientific research. In March, on the occasion of World Kidney Day, I asked our press office to interview leading colleagues in diabetology, immunology, endocrinology, hypertension and cardiovascular medicine and general practice about how they perceive CKD epidemics. From their replies, I noted their disposition towards furthering collaboration, but also the need to goconvincingly beyond the specialist vision of the problem.

Kidney health is still underestimated. What does the ERA-EDTA do to further raise awareness for kidney health? We take advantage of every possible opportunity to do this. National leaders are increasingly vocal in promoting public awareness of CKD. The ERA-EDTA is a partner in the European Kidney Health Alliance (EKHA). Together with the European Kidney Patients’ Federation, the European Dialysis and Transplant Nurses Association/European Renal Care Association (EDTNA/ERCA) and the International Federation of Kidney Foundations, the ERA-EDTA is deeply involved in promoting the issue of kidney health and disease at European level. One main function of EKHA is to maintain an interface with the European Commission and the European Parliament so that those institutions can play a powerful role in assisting national governments with the challenges posed by renal diseases. The present chair of EKHA, Professor Vanholder, a past ERA-EDTA President, is an excellent promoter of kidney health.

Looking into the future

Through a series of engaging conversations, world-renowned renal disease experts Professor David Wheeler (UK), Professor Mark Cooper (Australia) and Professor Peter Rosling (Denmark) will reveal what the future holds for the renal patient of tomorrow.

Today, 13:30–14:45, Meeting Room C1-M3
Lunch will be provided

Supported by an unrestricted educational grant from AstraZeneca Pharmaceuticals LP

In compliance with EBAC guidelines, all speakers/Chairpersons participating in this programme have disclosed or indicated potential conflicts of interest which might cause a bias in the presentations. The Organising Committee/Course Director is responsible for ensuring that all potential conflicts of interest relevant to the event are declared to the audience prior to the CME activities.

SGLT2 inhibitors of today for the renal patient of tomorrow:

Does the future look bright?

Following the non-dialysis pathway

Models of patient-centered comprehensive conservative management

Although the incidence of end-stage renal disease (ESRD) seems to have leveled off, elderly people represent a growing proportion of patients on dialysis. This population shows more comorbidity and lower functional status than younger patients, and even though survival might be longer with dialysis, the cost for the patient is reduction in quality of life and independence. Dialysis is a time-consuming treatment, which can lead to hospitalization caused by cardiovascular disease, infections and access problems. It has been found that even though patients may live longer, a substantial amount of that time is spent in hospital. Studies have shown that many elderly patients prefer quality of life over survival. For such patients, care without dialysis – comprehensive conservative management (CCM) – might be a better option than dialysis.

Patient-centered care is the main goal and requires shared decision making when discussing the future course of action, taking into consideration benefits, harms and patient preference and, when possible, involving next of kin. Patients who choose not to dialyze may be cared for by a multidisciplinary team using palliative-care principles that address physical symptoms, and social, psychological and existential needs. This can be achieved by collaboration between the patient’s nephrologist, nurse, primary care physician and specialized palliative care team, and involving, when necessary, psychologists, social workers and chaplain. In Denmark, this is a work in progress undertaken by a national collaboration of nurses and physicians from departments of nephrology all over the country.

Since 2012 a prospective, observational study has been carried out at the Department of Nephrology at Herlev Hospital, Denmark. At any given time, approximately 35 patients have been cared for without dialysis. The study currently includes 166 enrolled patients, of whom 122 have died. Two patients regretted their decision and died on hemodialysis (survival four and six months), four other patients had dialysis, (one while unconscious in the intensive care unit after surgery, three tried hemodialysis but stopped after one to three treatments). Overall, it shows that most patients who choose not to dialyze stand by their decision.

RES更加}\n
S 5.2
The nondialysis pathway in ESRD
Friday, 08:00–09.30, Auditorium 15
Membranous nephropathy (MN) is a major cause of nephrotic syndrome after the age of 50 years of age. It is characterized by the presence of immune deposits that consist of Ig reactive with podocyte antigens and of the membrane attack complex of complement (MAC). Three main podocyte antigens have been identified: neutral endopeptidase (NEP) in the neonatal form, phospholipase A2 receptor (PLA2R), and thrombospondin containing domain 7A (THSD7A) in the adult, where they account for 85% and less than 5% of the cases, respectively. Substantial advances have occurred in the last two years that will have significant impact on diagnosis and monitoring.

A new mouse model of THSD7A-related MN reveals new pathogenic pathways

To avoid the use of precious anti-THSD7A antibodies from patients, the Stahl group generated antibodies against the human and mouse orthologs of THSD7A in rabbits by coinoculation with the respective cDNAs. Injection of these antibodies into mice induced a severe nephrotic syndrome with the characteristic features of human MN. Surprisingly, MN developed in the absence of detectable complement activation. In vitro, anti-THSD7A antibodies caused cytoskeletal rearrangement and activation of focal adhesion signaling. Knockdown of the THSD7A ortholog in zebrafish larvae resulted in severe alteration of glomerular filtration barrier integrity.

A role for antibodies to complement regulatory proteins in disease progression

In primary MN, complement is usually activated by the lectin pathway, associated with super-activation of the alternative pathway (AP). In the experimental model of Heymann nephritis, antibodies to complement regulatory proteins (CRP) play an important role. Among CRPs, complement factor H (FH), a known AP inhibitor, contributes to the control of complement activation at the cell surface. We found anti-FH antibodies occurring in a patient with subsequent impairment of renal function in the absence of TMA. While anti-PLA2R antibodies disappeared, a high titer of anti-FH antibody was found in the serum. This IgG3 isotype auto-antibody recognized FH on Western blot, bound C-terminal domains CCP15-20, and inhibited FH binding to C3b. Whereas intense staining of FH contrasting with weak staining of properdin was detected in the first biopsy, the reverse occurred in the second biopsy—a finding compatible with slowly evolving AP hyperactivation. There was no sign of systemic complement activation, plasma FH antigenic level was in the normal range, and genetic analysis revealed no abnormality in FH and CFHR1-5 genes. Analysis of 92 sera from a retrospective study, they showed that immunization might be first directed against the immunodominant epitope CysR and then spread to additional epitopes in PLA2R. In a retrospective study, they showed that immunization might be first directed against the immunodominant epitope CysR and then spread to additional epitopes in PLA2R. We have confirmed this finding in our recent randomized controlled trial (GEMRITUX). Patients with reactivity with the immunodominant epitope CysR only, had a higher chance of spontaneous remission. By multivariate analysis, epitope spreading at baseline was an independent predictor of clinical remission at six months and last follow-up, irrespective of PLA2R-litter at baseline, age, gender, and treatment group. These data, which must be confirmed in other cohorts, suggest that additionally to anti-PLA2R antibodies, one should consider monitoring epitope reactivity profile once the relevant assay will be made commercially available.

Increased genetic complexity: trans-ethnic variations and epitope prediction

A pioneering study by a European consortium showed a highly significant genetic risk allele within HLA-QQA1. However, the biologically relevant class-2 molecule responsible for presenting peptides from PLA2R to the immune system could lie elsewhere in the HLA-D locus. This was shown by two Chinese research groups who identified 2 major alleles ORB1*1501 and ORB1*0301 in the context of larger haplotypes. The former seems to be specific for the Han population, whereas the latter is also at risk in the European population. Using predictive algorithms to identify which fragments of PLA2R would best fit within these variants, the Zhao group identified sequences within CTLD1 and CTLD7 PLA2R domains potentially linking the T cell and B cell epitopes of PLA2R. In a combined discovery and validation cohort, the Liu group found that nearly 99% of all PLA2R-associated MN carried either of the 2 alleles, and that individuals carrying one or both of these risk alleles had a 99-fold increased risk of PLA2R-associated MN versus healthy controls.

RESEARCH

Advances in the pathogenesis of membranous nephropathy

Recent studies will have significant impact on diagnosis and monitoring.
Epigenetics in CKD & CVD: A potential breakthrough therapy?

Introducing the INTEGRATED project
The quantitative and qualitative Impact of transitioning between RRT modalities

The INTEGRATED project is an international research consortium that intends to identify which patients will benefit from a given transition at a certain moment in time. Using a Delphi procedure to determine the scope of the project, the INTEGRATED group defined a set of different quantitative and qualitative questions that needed to be addressed.

From a quantitative viewpoint, the INTEGRATED group intends to provide evidence on the epidemiology, underlying causes and the timing and outcomes of different possible transitions between modalities, the risk factors leading to or predicting such transitions, and of the factors and practices that mediate the final outcome after the transition.

For this goal, an extensive international collaboration of registries was established, including ANZDATA, USRDS, CORR, DOPPS and ERA-EDTA registry; other registries are warmly welcomed to join. Such a collaboration is a substantial technical challenge, in view of the need to harmonize definitions within the different datasets. Common analytical plans will be run on the different registries.

In parallel with the quantitative approach, INTEGRATED will also address qualitative questions on the perceptions, beliefs and experiences of patients and physicians on the transitioning process between modalities. As a change process, it can be expected that a transition can lead to psychosocial distress in patients and their caretakers. It is postulated that the impact of the transition will be different depending on its timing (being urgent, unplanned versus planned), the readiness of the patient (prepared or not?), and the scope and extension of the change (e.g. will a new health care team need to be involved?). Furthermore, the transition from a home-based treatment, with a lot of freedom and responsibility for the patient, to a center-based treatment, with more directed and supervised care, can lead to conflicts and misunderstandings, and will also lead to more frustrations as there will be more disruption of lifestyle due to less flexibility. Last, the expertise and abilities of the team will be fundamental in determining whether or not the patient experiences the transition as successful.

The results of the large international research consortium INTEGRATED will contribute to a better qualitative and quantitative understanding of the process of transition, and by doing so improve the outcomes of patients with ESRD.
Although alkylating agents such as chlorambucil or cyclophosphamide are effective in the treatment of patients with membranous nephropathy, side effects limit their use. In the last decade, newer immunosuppressive agents have been introduced, such as mycophenolate mofetil (MMF), ACTH, calcineurin inhibitors (CNI: ciclosporin and tacrolimus) and rituximab. These newer drugs have fewer side effects, and if proven effective might replace cyclophosphamide as the primary choice of therapy in MN. There are few recent studies with MMF or ACTH. Although these agents can induce remission of proteinuria, there are no data to support their efficacy on hard renal endpoints compared to cyclophosphamide.

Calcineurin-inhibitors are already widely used in the treatment of membranous nephropathy. Only recently, a randomized controlled trial was published: this Indian study showed that tacrolimus was as effective as cyclophosphamide in inducing remission of proteinuria. Unfortunately, relapse rate after treatment withdrawal was higher with tacrolimus, likely reflecting limited long-term efficacy of a one-year course of CNI therapy. A longer treatment course might be more effective; however as yet there is no evidence to promote continued use of CNI for many years.

Rituximab has been studied in two recent randomized controlled trials. The French Gem-ritux study proved that rituximab increased remission rate compared to standard (control group) therapy. SKIL, more than 30% of patients did not develop remission after rituximab, confirming the non-response rate observed in other rituximab studies. The GEM- RITUX study also demonstrated that the KDIGO criteria to select patients at high risk of progression are insufficient: up to 60% of patients in the control group developed spontaneous remission.

Interestingly, recent studies have pointed to differences in efficacy between rituximab and cyclophosphamide, specifically in a subgroup of patients at highest risk of progressive disease: i.e. patients with very high levels of PLA2R antibodies. These data provide some perspectives for future treatment. The most important aspect is the recognition that current trials, guidelines, and treatment algorithms are targeting the 'average' patient. Measurement of PLA2R antibodies might allow the development of 'tailor made', patient-centered therapies. Patients with low or moderate risk of disease progression might initially be treated with rituximab or CNI, whereas cyclophosphamide might still be used in patients with high risk of disease progression. Treatment may be further improved by changing duration (shorter duration of cyclophosphamide, longer duration of CNI), intensity (intravenous cyclophosphamide, higher-affinity B cell therapy), or combination therapy. (sequential therapy, combinations of CNI + rituximab or low-dose cyclophosphamide + rituximab).
WHY BECOME A MEMBER?

ERA-EDTA is the leading European Nephrology Association that offers you exclusive advantages and opportunities.
Metabolic acidosis: Does correction prevent chronic kidney disease progression?

Metabolic acidosis is classified as a disorder of acid-base balance that results in a decrease of plasma bicarbonate concentration and in the lowering of pH. It is diagnosed in patients with chronic kidney disease (CKD) when the venous plasma or venous blood bicarbonate concentration is lower than 22 mmol/l. Since metabolic acidosis occurs frequently in CKD patients, bicarbonate concentration should be measured in venous plasma or venous blood in all these patients. Furthermore, because the incidence of metabolic acidosis increases with declining GFR, this procedure should be carried out at least once a year in patients with advanced CKD.

Metabolic acidosis is caused by impaired ammonium excretion, reduced tubular bicarbonate reabsorption and insufficient renal bicarbonate production. As the result of metabolic acidosis, numerous metabolic abnormalities develop, which may lead to dysfunction of several organs. In observational studies, CKD patients with metabolic acidosis are characterized by faster progression of kidney disease. As shown in the figure, results of animal experiments suggest that mechanisms involved in CKD progression induced by metabolic acidosis are: complement activation, stimulation of renin-angiotensin system activity and increased endothelin-1 and reactive oxygen species synthesis.

Results of clinical interventional studies suggest that, in CKD patients, alkali therapy (oral sodium bicarbonate or oral sodium citrate) slows progression of kidney disease. Treatment of metabolic acidosis with sodium bicarbonate appears to be safe. The existing data concerning the impact of the treatment of metabolic acidosis on CKD progression originate, however, from single-center, non-randomized studies that include only small groups of patients. Currently, three interventional studies involving a larger number of patients are being conducted.

Results of recent, short-term, clinical studies suggest that, when given orally, sodium-free hydrochloric acid binding agent – TRC101 – binds acids in intestines of CKD patients and is effective in treating metabolic acidosis. The long-term safety and renoprotective properties of therapy with this agent remain to be elucidated.

In addition to pharmacologic treatment, a diet rich in vegetables and fruits may have a beneficial effect on metabolic acidosis in CKD patients. Renoprotective effects of this diet have been reported in patients with CKD stages 1, 3 and 4. It should be kept in mind, however, that the use of a diet rich in vegetables and fruits can lead to hyperkalemia in patients with CKD. Careful selection of patients (i.e. those without a tendency to hyperkalemia) and close monitoring of serum potassium concentrations reduce the risk of hyperkalemia in these patients. It should also be noted that no studies have been conducted on the safety of a diet with an increased content of fruits and vegetables in CKD patients under the conditions of routine clinical practice (i.e. outside a clinical trial).

To summarize, currently, in CKD patients with metabolic acidosis, the use of oral sodium bicarbonate is recommended. Such therapy may slow CKD progression. The role of a diet enriched with base-producing fruits and vegetables and treatment of metabolic acidosis with TRC101 needs further study.
Too many advantages to list! We offer as many opportunities to our members as possible. Our CME courses are very popular – don’t miss our two for 2018. ‘Hands on Vascular Access’ in Copenhagen on May 24th and ‘How to become your local expert in Nephrogenetics’ in Serbia on October 8th/9th.

You have been YNP chair for nearly a year now. Looking back, what were your favorite moments and highlights? And what challenges or even drawbacks did you face?

It has all been very enjoyable and I feel very lucky to have had this opportunity! Organising a successful AKI course was hard work but very rewarding. Getting to working with a highly motivated group of individuals from different countries on the YNP board is great and I am very grateful to them all for their valuable input especially Muguet Koobasi, our project leader without whom we could not function! It can be challenging to introduce new initiatives and frustrating in terms of time delays but it is always nice when they are finally launched! We are keen to offer as many opportunities to our members as possible and are very happy to hear from anyone with any suggestions for new initiatives which they would like us to consider! Please get in touch.... ynp@era-edta.org

Young Nephrologists’ Platform: We are keen to offer as many opportunities to our members as possible.

Why is the YNP important and should be known by any nephrologist under the age of 40?
The YNP is important because young nephrologists are the future and therefore it is imperative that they are supported in a forum where their specific needs can be addressed. We need to engage younger nephrologists to participate more actively within the ERA. The YNP strives to make nephrology accessible and to support current nephrologists in terms of education and experience.

What are the advantages of a YNP membership – and why is networking so important for young doctors?
Too many advantages to list! We offer a number of initiatives to support young nephrologists; these include free ERA membership, annual CME courses with heavily discounted registration, access to free registration and discounts for other courses, the opportunity to review for NDT and cjk, funding to invite a YNP member to speak at National Society meetings, an advisory programme, the opportunity to speak at The ASN. We select speakers from our membership to present at the annual congress which is a great opportunity and we hold a reception at the annual congress to allow members to meet in an informal setting and this year, certificates will also be awarded to those who have successfully passed the ECN examination. Full details of all our initiatives can be found on our webpage (http://web.era-edta.org/young-nephrologists-platform-ynp)

What steps do you take to further increase the number of members?
Membership of the YNP is now automatic when you join The ERA as a member aged < 40 years, unless you opt out. Although why would you?

What are the most important projects of the YNP?
They are all important and they are designed and selected to appeal to as broad an audience as possible. Our CME courses are very popular – don’t miss our two for 2018. ‘Hands on Vascular Access’ in Copenhagen on May 24th and ‘How to become your local expert in Nephrogenetics’ in Serbia on October 8th/9th.

You will learn how renowned nephrology experts Professor Biff Palmer (USA), Professor Roberto Pecoits-Filho (Brazil) and Professor Iain Macdougall (UK) would manage Mr Andersen’s hyperkalaemia and renal anaemia.
Can antidiabetic drugs prevent CKD progression? The benefits of SGLT-2 inhibition may extend beyond diabetes

The benefits of SGLT-2 inhibition may extend beyond diabetes and initiation of renal replacement therapy (RRT) by 46% (HR 0.54, 95% CI 0.40–0.75) in the EMPA-REG Outcome study. Even in the subgroup with nephrotic-range proteinuria, the annual loss of eGFR was reduced from 10.7 to 4.5 ml/min/1.73 m² [3]. In CANVAS/CANVAS-R, canagliflozin 100–300 mg/d had a similar-sized effect on the composite renal outcome of a 40% reduction in eGFR and initiation of RRT (HR 0.60, 0.47–0.77). However, it is not possible to draw definite conclusions about any beneficial effects of SGLT-2 inhibition on kidney disease progression in CKD in these exploratory analyses, and dedicated diabetes and CKD trials are expected.

The mechanism of action of SGLT-2 inhibitors targets the kidney and causes about half of filtered glucose and a few mmol of sodium to be excrated, accompanied by an osmotic diuretic effect of glycosuria. As a byproduct, this effect may modify cardiovascular risk through reductions in plasma volume, organ congestion and systemic blood pressure, and may be particularly beneficial at preventing heart failure. It all starts in the kidney and nephrologists by training can particularly understand how SGLT-2 inhibition restores delivery of sodium to the macula densa, promoting adenosine production and afferent arterial vasoconstriction.[4] Importantly, these effects do not appear dependent on RAS blocker, thiazide or loop diuretic use.

Most important are safety aspects, especially with no higher risk of hypoglycaemia, hyperkalaemia or acute kidney injury. All SGLT-2 inhibitors increase the frequency of mycotic genitourinary infections by about three-fold, but do not increase urinary tract infection. With canagliflozin, the possibility of an increased risk of amputation and fracture risk was raised and will be carefully monitored in ongoing trials (DECLARE, VERTIS CV, CREDiT, DAPA-CKD, EMPA-Kidney, EMPEROR preserved and EMPEROR reduced, Dapa-HF).

In summary, the increased sodium delivery to the macula densa seems to reduce intra-glomerular pressure and may account the apparent reductions in albuminuria and the rate of kidney function decline. Importantly, these effects appear to be maintained at lower levels of kidney function despite attenuation of glycosuric effects, and may not be dependent on diabetic levels of hyperglycaemia. There may therefore be a rationale of studying the effects of SGLT-2 inhibition on the progression of chronic kidney disease regardless of whether or not people have diabetes mellitus.

References
03. Ruggenenti et al, ERA-EDTA May 26, SP145

S 4.2 Progression of chronic kidney disease – hot issues beyond blood pressure and renin-angiotensin system
Friday, 11.45 – 13.15, Hall A2

Transfer to hemodialysis was not significant more common in the control group (27%) than in the retraining group (21%). Nor did the duration of peritonitis-related hospital care differ between the groups. The power of the study might have been lower than planned, since the discontinuation rate in the study was higher and the peritonitis rate in the control group was lower than expected.

In conclusion, this trial did not show that the ‘new model of follow-up’, that included regular targeted testing and retraining of new PD patients, could prolong time to first peritonitis, reduce the risk of peritonitis and transfer to haemodialysis, or shorten the time of peritonitis-related hospitalization.

References

S 6.2 Optimising clinical outcomes and technique survival
Friday, 08:00 – 09.30, C1-M1-2

What we have learned from the Peritonitis in Peritoneal Dialysis

Peritonitis is an important and potentially serious complication in patients treated with peritoneal dialysis (PD) because it increases the risks of technique failure and mortality. Previous studies have found that PD patients who are non-adherent to the PD protocol more often experience a peritonitis episode than adherent patients. In a large Italian study, 29% of PD patients were estimated to need retraining in PD exchange technique.[1] Observational studies indicate that retraining of PD patients can reduce the peritonitis rate, but this has not been confirmed by a controlled study.

The aim of the randomized controlled Prevention of Peritonitis in Peritoneal Dialysis (PEPS) study was to investigate if a new model of follow-up of new PD patients – involving testing of their theoretical knowledge and practical skills with a focus on infection prophylaxis – could, compared with standard treatment, reduce time to first peritonitis, the rates of overall peritonitis, and PD technique failure, and duration of peritonitis-related hospitalization. The study was undertaken from January 2010 to December 2015, and included 671 new PD patients at 57 hospitals in Sweden, Denmark, Norway, Finland, Estonia, Latvia, the Netherlands and the UK. Patients were randomized to a control group (n = 331), who were treated according to the routine practice of each center, or a retraining group (n = 340), who underwent testing at one, three and six months after PD start and every six months thereafter up to 36 months. Patients performed a practical test, with focus on PD exchange technique, and filled out a questionnaire that focused on infection prophylaxis. If the goals of the tests were not reached, retraining was given. The number of patients who completed 12 and 36 months of follow-up were 67% and 13% versus 57% and 9% in the control and retraining group, respectively. The main reasons for discontinuation from the study were kidney transplantation and transfer to hemodialysis. A first peritonitis episode was experienced by 30% of the retraining group and 37% of the control group, but time to first peritonitis was not significantly longer in the retraining group than in controls (p = 0.52). Older age, higher body mass index and higher number of PD bags changed per day were significant risk factors for a first peritonitis episode (p < 0.001). The overall peritonitis rate per treatment year was 0.333 episodes in the retraining group and 0.357 episodes in the controls, corresponding to 36.0 and 33.7 months per peritonitis episode. This did not differ between the groups (p = 0.63).

transfer to hemodialysis was not significant more common in the control group (27%) than in the retraining group (21%). Nor did the duration of peritonitis-related hospital care differ between the groups. The power of the study might have been lower than planned, since the discontinuation rate in the study was higher and the peritonitis rate in the control group was lower than expected.

In conclusion, this trial did not show that the ‘new model of follow-up’, that included regular targeted testing and retraining of new PD patients, could prolong time to first peritonitis, reduce the risk of peritonitis and transfer to haemodialysis, or shorten the time of peritonitis-related hospitalization.

References

S 6.2 Optimising clinical outcomes and technique survival
Friday, 08:00 – 09.30, C1-M1-2

Can a new glucose-lowering medication, such as the sodium-glucose co-transporter-2 (SGLT-2) inhibitors, really be called ‘antidiabetic drugs’ when they prevent progression of diabetic kidney disease despite only modest improvements in glycemic control? The title of this presentation, as selected by the scientific committee of this year’s ERA-EDTA congress, is provocative and indirectly, or rather directly, addresses nephrologists to critically discuss the potential cardio-renal benefits of SGLT-2 inhibitors seen in the EMPA-REG Outcome study results or more recently the pooled CANVAS/CANVAS-R program. In the 7,020 and 10,142 participants, respectively, empagliflozin or canagliflozin reduced HbA1c by about 0.4–0.6% [1, 2]. In dapagliflozin studies, HbA1c differences were attenuated to ~0.3% among those with lower levels of kidney function, and even less in people with eGFR between 30 and 60 ml/min/1.73 m².

Despite this, empagliflozin 10–25 mg/d reduced the incidence of the traditional renal composite outcome of doubling of creatinine and initiation of renal replacement therapy (RRT) by 46% (HR 0.54, 95% CI 0.40–0.75) in the EMPA-REG Outcome study. Even in the subgroup with nephrotic-range proteinuria, the annual loss of eGFR was reduced from 10.7 to 4.5 ml/min/1.73 m² [3]. In CANVAS/CANVAS-R, canagliflozin 100–300 mg/d had a similar-sized effect on the composite renal outcome of a 40% reduction in eGFR and initiation of RRT (HR 0.60, 0.47–0.77). However, it is not possible to draw definite conclusions about any beneficial effects of SGLT-2 inhibition on kidney disease progression in CKD in these exploratory analyses, and dedicated diabetes and CKD trials are expected.

The mechanism of action of SGLT-2 inhibitors targets the kidney and causes about half of filtered glucose and a few mmol of sodium to be excrated, accompanied by an osmotic diuretic effect of glycosuria. As a byproduct, this effect may modify cardiovascular risk through reductions in plasma volume, organ congestion and systemic blood pressure, and may be particularly beneficial at preventing heart failure. It all starts in the kidney and nephrologists by training can particularly understand how SGLT-2 inhibition restores delivery of sodium to the macula densa, promoting adenosine production and afferent arterial vasoconstriction.[4] Importantly, these effects do not appear dependent on RAS blocker, thiazide or loop diuretic use.

Most important are safety aspects, especially with no higher risk of hypoglycaemia, hyperkalaemia or acute kidney injury. All SGLT-2 inhibitors increase the frequency of mycotic genitourinary infections by about three-fold, but do not increase urinary tract infection. With canagliflozin, the possibility of an increased risk of amputation and fracture risk was raised and will be carefully monitored in ongoing trials (DECLARE, VERTIS CV, CREDiT, DAPA-CKD, EMPA-Kidney, EMPEROR preserved and EMPEROR reduced, Dapa-HF).

In summary, the increased sodium delivery to the macula densa seems to reduce intra-glomerular pressure and may account the apparent reductions in albuminuria and the rate of kidney function decline. Importantly, these effects appear to be maintained at lower levels of kidney function despite attenuation of glycosuric effects, and may not be dependent on diabetic levels of hyperglycaemia. There may therefore be a rationale of studying the effects of SGLT-2 inhibition on the progression of chronic kidney disease regardless of whether or not people have diabetes mellitus.
Controversies surrounding RAASi treatment and hyperkalaemia in cardio-renal patients

Chair: Professor John Cunningham

Friday 25 May 2018
13:30–14:30
Bella Center Copenhagen
Hall A2

PROGRAMME

13:15    Lunchboxes will be provided
13:30    Welcome and introduction
         Professor John Cunningham (UK)
13:35    Pathophysiology of recurrent hyperkalaemia
         Professor Biff F. Palmer (USA)
13:50    RAASi benefits in slowing down kidney function decline
         Professor Laurent Juillard (France)
14:05    New treatment options in hyperkalaemia management
         Professor Bertram Pitt (USA)
14:20    Roundtable discussion and meeting close
         All
The DOPPS Program Research Symposium

Optimizing care in advanced CKD and dialysis with a focus on diabetic patients: “The sweet truth”

The three studies in the DOPPS Program enroll national samples of clinics or dialysis units, collect detailed patient-level and facility-level data, and employ statistical modelling approaches to minimize treatment by indication bias. Through these efforts, the ultimate goal of the DOPPS Program is to inform best practices leading to improvements in care that allow patients to live longer with better quality of life.

The DOPPS Program is made possible through generous support by a consortium of biopharmaceutical and government sponsors that provide their support without restriction on publications, now numbering well over 200. It is the many contributions and devoted efforts of more than 100 investigators, study team members, clinical research associates, hundreds of dialysis unit staff, and more than 100,000 patient participants across over 20 countries who together provide findings from the DOPPS Program to help improve care for advanced CKD and dialysis patients worldwide. The DOPPS Program is committed to new collaborations to maximize its value as a resource for the community. Visit www.dopps.org to learn more about opportunities for research collaboration or for your country to join the DOPPS Program.

The DOPPS Program is honored and very appreciative of the opportunity once again to share its international findings with attendees of the ERA-EDTA Congress in an interactive session that we hope encourages and nurtures opportunities for new clinical initiatives and research. The symposium is moderated by Bruce Robinson, CKDopps Germany country investigator and Bruce Robinson, Principal Investigator of the DOPPS Program since 2009.

The burden of diabetes in advanced CKD and dialysis (Bruce Robinson)

In keeping with the scientific focus on diabetes at the 2018 ERA-EDTA Congress, the DOPPS symposium will address optimal care for our patients with diabetes and common comorbidities, such as hypertension. Not only does diabetes drive much of the burden of advanced CKD and ESKD across the globe, it remains a major determinant of clinical complications and mortality in this population. After Dr. Robinson launches the symposium with an overview of the burden of diabetes in advanced and ESKD, the ensuing four speakers will speak to management conundrums and solutions in these patients.

DOPPS: Hepatitis C in HD patients – prevalence trends over 20 years, outcomes, and use of newer treatments (Michel Jadoul)

Dr. Jadoul will review the most recent findings regarding Hepatitis C virus (HCV) infection in in-center HD patients. HCV can now be cured in > 95% of HD patients by recently available Direct-Acting Antiviral agents (DAA). Surprisingly, there is a dearth of data regarding trends in the prevalence and incidence of HCV in HD patients over the last decade. We therefore queried the DOPPS database to assess the prevalence of HCV and found that, among countries in the DOPPS since the initial phase of data collection, HCV prevalence decreased from 14% (1996–2001) to 8% (2012–2015), while HCV incidence dropped from 2.9 to 1.2 cases per 100 patient years. Extrapolated to the global HD population that exceeds 1.5 million, this still corresponds yearly to a minimum of 20,000 cases acquired on HD.

In the absence of molecular virology data on HCV strains, nosocomial transmission cannot be demonstrated but appears from multiple arguments to represent the main cause of HCV seroconversion. Indeed, whereas most HD units in the DOPPS do not experience a single case of HCV seroconversion, around 10% of units experience 3 or more cases. These mini-outbreaks are suggestive of lapses in hygienic precautions. Although blood transfusions have historically been an important contributor to HCV transmission to HD patients, these procedures are now extraordinarily safe (and relatively rare) in most DOPPS countries and no longer play a significant role.

Finally, we took advantage of the large cohort of incident HD patients in the DOPPS to assess the prevalence of HCV among patients enrolling in the study within 4 months of starting HD. Because mounting HCV antibodies requires 5 or more months in HD patients, the prevalence of HCV after < 4 months on HD largely corresponds to HCV infections acquired prior to HD start. HCV prevalence among these patients (~5%) was much greater than in the age-matched general population of the corresponding countries. Thus, eradicating HCV from HD units will require careful screening and DAA treatment of incident HD patients. In this respect, despite highly effective DAA regimens, treatment rates were very low in the DOPPS, although the most recent data show a “thrill” towards greater treatment rates.

Overall, these results point to the need for reinforcement of hygienic precautions in HD units, together with an obligation to dramatically increase DAA treatment rates of HCV+ patients. This appears as a readily available way to get rid of the substantial HCV-associated morbidity and mortality. Treating HCV-infected patients would further reduce the HCV reservoir and thus the risk of nosocomial transmission.

CKDopps: Diabetes treatment, control, and hypoglycemia in patients with advanced CKD (Benedicte Stengel)

Although diabetes is the leading cause of CKD, little is known about practice patterns of anti-diabetic therapy at low eGFR levels and its correlation with glycemic control. CKDopps is an ongoing international prospective cohort study in national samples of nephrology clinics in Brazil, France, Germany, Japan, and the United States, with an overall goal to study variations in advanced CKD practices to identify nephrologist practices associated with better patient outcomes. Dr. Stengel will give an overview of CKDopps study findings relating to current anti-diabetic treatment and glycemic control in the study’s national samples in participating countries. Descriptive data will demonstrate important variations in practice patterns of anti-diabetic therapy across countries. Characteristics of patients with diabetes will be described, as well as glycemic control according to CKD stage.

EURODOPPS: Outcomes according to different strategies of HbA1c use among diabetic HD patients (Ionut Nistor)

The EURODOPPS is a collaborative venture between the ERA-EDTA and Arbor Research Collaborative for Health, which organizes the DOPPS Program. The aims of EURODOPPS are to provide investigators access to DOPPS data in several participating European countries (Germany, Italy, France, United Kingdom, Belgium, Spain, and Sweden) and provide aid in epidemiological analysis to address scientific and policy-related questions. Details are at www.era-edta-reg.org/EURODOPPS.
In the four years since its conception, the EURODOPPS initiative has provided an opportunity for seven European investigators to analyze the EURODOPPS data, culminating in seven projects from two calls for research proposals. With nearly all research projects from the first call coming to completion, the EURODOPPS project has so far published two papers, with others in the submission process.

Dr. Nistor will present findings from his EURODOPPS project that explored whether glycosylated hemoglobin A1c (HbA1c) targets and their attainment differ widely across European dialysis centers, as well as among clinical practice guidelines. The impact of different fidelity practices related to HbA1c management on all-cause and cardiovascular mortality and time to first hospital admission in 3,679 HD patients with type 2 diabetes mellitus in EURODOPPS phases 4 and 5 (2009–2015) was analyzed. Preliminary results do not support the notion that using well-defined specific HbA1c targets as a tool to manage glyemic control improves outcomes in European diabetic patients on HD.

Dr. Nistor will present findings from his EURODOPPS project that explored whether glycosylated hemoglobin A1c (HbA1c) targets and their attainment differ widely across European dialysis centers, as well as among clinical practice guidelines. The impact of different fidelity practices related to HbA1c management on all-cause and cardiovascular mortality and time to first hospital admission in 3,679 HD patients with type 2 diabetes mellitus in EURODOPPS phases 4 and 5 (2009–2015) was analyzed. Preliminary results do not support the notion that using well-defined specific HbA1c targets as a tool to manage glyemic control improves outcomes in European diabetic patients on HD. Over decades, strategies to minimize or eliminate steroids have been developed to improve the metabolic profile. However, the inconsistencies in these protocols and the chronic graft dysfunction observed in some steroid-free treated patients have resulted in low usage of this regimen in several centers. One possible explanation why steroid-free immunosuppression may fail is suggested by the OSAKA trial, in which a higher incidence of graft dysfunction was reported in the steroid-free arm. A sub-analysis revealed that steroid avoidance may have a greater negative impact on kidneys from expanded-criteria donors, and therefore it is likely that only low-immunologic-risk recipients of expanded-criteria donor kidneys may benefit from a steroid-avoidance regimen. The large ADVANCE trial has very recently shown that steroid avoidance is associated with 5% more acute rejection as compared to the 10-day steroid withdrawal arm. Chronic calcineurin inhibitor (CNI) nephrotoxicity has been suggested as a major obstacle to long-term allograft survival, and thus several attempts have been made to minimize or convert CNI to improve the long-term outcome. CNI withdrawal, minimization or avoidance protocols have been conducted using mycophenolic acid and/or mammalian-target-of-rapamycin (mTOR) inhibitors and/or belatacept. Despite promising short-term results, these approaches have failed, and more acute rejections and de novo donor-specific antibodies formations have been observed in CNI-free regimens. Of note, a minority of kidney transplant recipients may benefit from a CNI-free regimen, but identifying this cohort remains highly speculative and our experience is limited to clinical case observations. Despite excellent results with “minimal” tacrolimus exposure along with other immunosuppressants, the question remains about which “low” level is safe, since the low tacrolimus level was in fact higher than intended in the SYMPHONY study.

There have also been several attempts to reduce maintenance immunosuppression while using induction immunosuppression with depleting antibodies. However, a depleting agent alone was not enough for successful minimization of tacrolimus monotherapy, even in preselected patients. The sequential double induction protocol based on alemtuzumab and infliximab followed by tacrolimus monotherapy in the proof of concept trial showed promising five-year outcome even in T-cell presensitized patients, and a validation trial is ongoing.
Anti-GBM disease: new subgroups and novel therapies

MÅRTEN SEGELMARK
Linköping, Sweden

For many years anti-GBM disease was thought to be the only kind of glomerulonephritis driven by autoantibodies. Now it has become evident that autoantibodies also play an important part in ANCA-associated nephritis, membranous nephropathy and IgA-nephritis. This has renewed the interest in anti-GBM as a model for autoimmune kidney diseases.

The development of toxic anti-GBM autoantibodies requires both B-cells and T-cells. For two decades, it has been known that B-cells react with cryptic epitopes on the non-collagenous domain of the C3 chain of type IV collagen, and that carriers of the HLA-DR15 have an increased risk of developing anti-GBM disease. It has been shown that there is a peptide sequence in the NC1 domain of T-cells that recognize, which is necessary for the development of nephritis. Recently Richard Kitching’s group in Australia showed that this peptide was presented differently by HLA-DR1 and DR15 molecules. DR15 presentation of the nectinophilic peptide promoted the development of T-helper cells, while DR1 presentation of the peptide promoted the development of regulatory T-cells.

The discovery of the B-cell epitopes led to the development of rapid immunoassays for the detection of circulating anti-GBM. This has enabled early diagnosis, which has had an impact on the prognosis. There are cases, however, where commercial assays are negative even if anti-GBM are clearly present on renal biopsy. Often circulating antibodies can be detected by alternative special techniques.

We recently described a group of patients with no or very low reactivity in standard assays, where most autoantibodies were of the subclass IgG. Interestingly these patients were all young females smokers, with predominately pulmonary involvement.

A large percentage of patients with anti-GBM disease also have myeloperoxidase-ANCA (MPO-ANCA). As a group, double-positive patients are older, and they have more profound symptoms. This opens up a window of opportunity for early diagnosis, but it is questionable if double-positive patients have a better overall renal prognosis. The clinical most important aspect of double positivity is the increased relapse risk, making maintenance immunosuppressive therapy warranted for double-positive patients.

There are several reports of overlap between membranous nephropathy and anti-GBM disease. Such patients usually have nephrotic-range proteinuria in combination with crescentic glomerulonephritis. It has been suggested that membranous nephropathy might trigger an autoimmune response against the cryptic anti-GBM epitopes. However, there are no cases described with simultaneous anti-PLAZR antibodies and antibodies to type IV collagen. An alternative explanation is that some anti-GBM antibodies preferentially deposit on the subepithelial side of the GBM, thereby mimicking the immune complexes seen in membranous nephropathy.

Cyclophosphamide is today the standard therapy to stop the autoantibody production. Histological data indicate that cyclophosphamide substantially shortens the time circulating antibodies are present. This reduces the risk of glomerulonephritis and pulmonary haemorrhage, and enables renal transplantation at an earlier time point. In ANCA-associated vasculitis it has been shown that targeting B-cells with rituximab leads to a more rapid decline of circulating antibodies. There are reports of the use of rituximab in anti-GBM disease, but no head-to-head comparison.

Cyclophosphamide is today the standard therapy to stop the autoantibody production. Histological data indicate that cyclophosphamide substantially shortens the time circulating antibodies are present. This reduces the risk of glomerulonephritis and pulmonary haemorrhage, and enables renal transplantation at an earlier time point. In ANCA-associated vasculitis it has been shown that targeting B-cells with rituximab leads to a more rapid decline of circulating antibodies. There are reports of the use of rituximab in anti-GBM disease, but no head-to-head comparison.

Plasma exchange is used to lower levels of circulating autoantibodies. However, each session only removes about one third of the IgG in the body. Thus it takes several days to reach non-toxic levels. Immunoabsorption techniques have been employed as an alternative. This leads to a more rapid decline of the antibodies, but it is not clear in how many patients this method has made a difference in outcome. The streptococcal enzyme IdeS degrades all IgG in the body in less than 15 minutes. In animals it can also de-grade IgG bound the GBM. We are now conducting a study to evaluate the potential of IdeS in anti-GBM disease (ClinicalTrials.gov NCT03157037).

In conclusion, the renewed interest in anti-GBM disease, spurred by the detection of autoantibodies in other forms of glomerulonephritis, has led to an exciting development in studies on pathogenesis as well as diagnosis and management.

References


S 3.5 Lupus and vasculitis – recent advances in therapy
Friday, 15.00–16.30, Hall A2

Tubular handling of calcium and magnesium: Recent insights from genomewide association studies

OLIVIER DEVUYST
Zurich, Switzerland

The kidneys play a major role in the homeostasis of calcium and magnesium: in steady state, 98% of the filtered Ca2+ and 95–99% of the filtered Mg2+ are reabsorbed by the nephron. The handling of Ca2+ and Mg2+ involves a transcellular pathway, mediated by specific transporters expressed in tubular cells, and a paracellular pathway that depends on transcellular electrochemical gradients and is regulated by specialized junctional proteins, the claudins. Despite progress in the identification of the transport systems involved, many fundamental issues related to the handling of Ca2+ and Mg2+ remain unresolved. In this lecture, we will summarize recent studies that shed light on genetic factors and molecular mechanisms governing the pathways involved in the tubular re-absorption of Ca2+ and Mg2+, and the link between Mg2+ homeostasis and metabolic disorders.

Estimating the heritability of a given trait (i.e. the degree of variation of a trait in a population) is due to genetic variation between individuals in that population) is the first step in gene discovery. The heritability of renal clearances for electrolytes in the general population was previously unknown. Based on a multicenter population cohort from Switzerland (N = 1,128), we showed significant heritability values for serum concentration of Ca2+ and Mg2+ (37% and 33% respectively) and for 24-hour urine clearance for Ca2+ and Mg2+ (45% and 27% respectively). The heritability for eGFR was 46% (CKD-EPI equation) in this population. These results paved the way for identifying genetic variants involved in Ca2+ and Mg2+ homeostasis in the general population.

Genome-wide association studies (GWAS) represent an essential tool to uncover genetic regions associated with renal function parameters. The success of GWAS was built on their conceptual simplicity and hypothesis-free, unbiased approach. Typically, genetic variants uncovered through GWAS are associated with a relatively small effect size, and their identification requires large study populations. The results of the first GWAS addressing the tubular handling of Mg2+ and its potential influence on metabolic traits in the general population have recently become available. The analysis of 9,099 individuals from seven cohorts evidenced two loci associated with urinary magnesium: TRPM6, which encodes a Mg2+ channel, and ARL15, a GTP-binding protein that was shown to regulate TRPM6 currents in kidney cells and to regulate Mg2+ handling and metabolism in zebrafish. Genetic variants in ARL15 modified the association of urinary Mg with fasting insulin and fat mass in a general population.

A second GWAS that investigated the urinary Mg2+ to Ca2+ ratio in 9,320 adults from four genetic isolates and three urban cohorts evidenced a top locus encompassing CLDN14, the gene coding for claudin-14. Claudin-14 is a tight junction protein expressed in tubular segments handling Mg2+; it has been associated with kidney stones and its expression is regulated by changes in dietary Mg2+ content.

These studies, which combine population genetics with observational and experimental approaches, uncovered a gene-environment interaction linking Mg2+ deficiency to insulin resistance and obesity. They highlight the power of urinary electrolyte ratios to unravel genetic determinants of renal tubular function.

References


S 1.1 Renal physiology – tubular transport
Friday, 15.00–16.30, Auditorium 15

View the ERA-EDTA 2018 Broadcast on the YouTube playlist here.
VISIT OUR BOOTH at # 2.291

Some of our key leaders will explain in detail all the Association’s activities and answer your questions.
Balancing perspectives: The ASN Lecture – Highlights in ESRD

VANDANA DUA NIYYAR
Atlanta, United States of America

The American Society of Nephrology (ASN) Highlights in End Stage Renal Disease lecture will cover updates in the field of dialysis, as presented at the ASN annual meeting in New Orleans in 2017. Attention will be focused on the late-breaking clinical trials section, and preliminary results of novel innovative technologies for vascular access creation will be discussed. Pragmatic clinical trials conducted under real-world conditions are increasingly being performed, as their findings are generalizable to clinical practice, and cost less than trials that require extensive research infrastructures. The TiME trial was an NIH-funded pragmatic trial that aimed to look at the impact of increasing time on dialysis on patient-centered outcomes including mortality, hospitalization rate and quality of life (not published yet). The results and conclusions of the trial will be emphasized.

Additionally, preliminary data from a Phase 2 single-arm trial, with bioengineered human acellular vessels for dialysis access will be presented. [2] Allogenic cells were used to grow bioengineered vessels in bioreactors, and were then decellularized. The tissue-engineered vascular grafts averaged 6 mm in diameter and 40 cm in length, and were surgically implanted in 60 patients. The first human clinical experience with these grafts will be detailed, including primary and secondary patency.

Finally, putting all this into perspective for the dialysis patient and balancing provider and patient-centered outcomes is key. The SONG-initiative (Standardized Outcomes in Nephrology) was formed to develop core outcomes across the spectrum of chronic kidney disease, based on priorities from patients, caregivers, clinicians, policymakers, researchers, and industry. SONG-HD focuses on hemodialysis,[3] and qualitative analyses of the workshop discussion with guidelines for implementation will be presented.

References
This presentation will have something for everyone and could be titled: “Everything you want to know about the Kidney Week transplantation talks in 22 minutes or less”!

Dr Michelle Josephson’s lecture entitled ASN Highlights: Transplantation’ provides the best parts of clinically relevant transplantation topics and lectures presented at the 2017 American Society of Nephrology Kidney Week Meeting, held in New Orleans, Louisiana, October 31st – November 5th 2017. The lecture, a Kidney Week transplantation topics overview, will include areas relevant to both pre-transplant evaluation and post-transplant management. For pre-transplant evaluation, the topics will include: emerging strategies that provide more useful and predictive transplant candidate evaluations, such as (our developing appreciation of) the impact of pre-transplant frailty on post-transplant outcomes; evolving efforts to construct risk calculators that quantify wait list and post-transplant risk; and the role of, and rationale for, screening for malignancy prior to transplant. Pre-transplant treatment with Ides to enable transplantation in highly sensitized individuals will be included. Post-transplant management issues to be discussed include: which malignancies increase in incidence after transplant and which do not; recommendations regarding post-transplant screening; infection and vaccination post-transplant; a brief discussion of hepatitis B and C; and a segment on belatacept.

The last will include key findings from the seven-year follow up on the BENEFIT Trial, as well as real-world experience with using belatacept, and how the growing understanding of the drug in practice has shaped clinical protocols. Post-transplant monitoring topics include key points from presentations that discussed what we have and can learn from protocol biopsies, whether or not to monitor for donor-specific antibodies and some developing treatments, such as what is new on the co-stimulation blockade horizon and information about the new shingles vaccine. The areas covered are clinically important and of interest to both the general nephrologist and the transplant nephrologist.
Glomerular disease and podocytopathies: novel and evolving regimens

New mono- and combination therapies offer hope for better outcomes for patients

JAMES TUMLIN
Atlanta, United States of America

The diagnosis and management of glomerular diseases and their risk for progressive renal disease remain a challenge for the global nephrology community. The broad range of glomerular disorders, including both immune complex and non-complex forms, requires the clinician to have a working knowledge of multiple treatment options.

Historically, standard treatments for the majority of glomerular diseases involve some form of immunomodulation due to the assumption that dysregulated immunity is central to the disease pathogenesis. While immunosuppression is effective in a number of glomerular diseases, the response can be variable and ultimately dependent on individual patient conditions. For example, the seminal observations by Beck et al and others have shown that anti-PLA2 antibodies are a causative in the development of membranous glomerulopathy (MGN) and that reducing antibody titers correlates with a reduction in proteinuria.[1]

However, subsequent observations by Ruggenent et al[2] and others suggest that B-cell-directed therapies may not be sufficient to induce a complete remission. Consistent with these observations, pre-clinical studies find that many drugs used in the treatment of glomerular diseases reduce proteinuria due to direct effects on podocyte function as opposed to immunomodulation. These observations suggest that treatment of glomerular diseases should involve the broader concept of combining immunomodulation therapies with treatments designed to stabilize podocyte function in concert with agents that are able to preserve podocyte viability.

During this meeting, we will hear the lecture entitled ‘Glomerular disease and podocytopathies: Novel and evolving treatment regimens’, which will review evolving immunosuppressive and non-immunologic treatment for FSGS. The MENTOR trial is a ground-breaking trial comparing the complete or partial remission rates at 24 months in patients with idiopathic MGN who were randomized to either oral cyclosporin (CsA) or intravenous (IV) rituximab. In this study, IV rituximab was shown to not only be non-inferior to CsA in inducing complete or partial remission rates, it was also able to reduce the incidence of clinical relapse.

The concept of using combination drug therapy that modifies different cellular pathways in order to minimize toxicity has been increasingly used in the treatment of glomerular diseases. The DUET trial examined the efficacy of sparsentan (a selective antagonist of the endothelin alpha receptors) in combination with irbesartan therapy in patients with FSGS, and demonstrated an effective non-immunologic method for reducing proteinuria. Lasty, ACTH has been successfully used in combination with oral tacrolimus to induce complete or partial remissions in a group of multidrug-resistant FSGS and MGN patients. The growing therapeutic options for treating glomerular disease alone or in combination offers hope in the treatment of all forms of glomerular disease.[3]

References

Proteasuria: the primary mechanism of sodium retention and edema in proteinuric kidney disease

SODIUM RETENTION AND EDEMA FORMATION ARE TYPICAL FEATURES OF PATIENTS WITH PROTEINURIC KIDNEY DISEASE AND NEPHROTIC SYNDROME. RECENTLY, BASED ON IN VITRO DATA, ACTIVATION OF THE EPITHELIAL SODIUM CHANNEL (ENaC) BY ABERRANTLY FILTERED SERINE PROTEASES HAS BEEN PROPOSED AS THE UNDERLYING MECHANISM.[1] RECENTLY, THIS CONCEPT WAS PROVED IN VIVO IN NEPHROTIC MICE THAT WERE PROTECTED FROM PROTEOLYSIS BY ANTI-PLA2 (PLA2G3) ANTAGONISTS, SUGGESTING THAT DYSREGULATED IMMUNITY IS CENTRAL TO THE DISEASE PATHOGENESIS. WHILE IMMUNOSUPPRESSION IS EFFECTIVE IN A NUMBER OF GLomerular DISEASES, THE RESPONSE CAN BE VARIABLE AND ULTIMATELY DEPENDENT ON INDIVIDUAL PATIENT CONDITIONS. FOR EXAMPLE, THE SEMINAL OBSERVATIONS BY BECK ET AL AND OTHERS HAVE SHOWN THAT ANTI-PLA2 ANTIBODIES ARE A CAUSATIVE IN THE DEVELOPMENT OF MEMBRANOUS GLomerULOPATHY (MGN) AND THAT REDUCING ANTIBODY TITERS CORRELATES WITH A REDUCTION IN PROTEINURIA.[1]

HOWEVER, SUBSEQUENT OBSERVATIONS BY RUGGENENT ET AL[2] AND OTHERS SUGGEST THAT B-CELL-DIRECTED THERAPIES MAY NOT BE SUFFICIENT TO INDUCE A COMPLETE REMISSION. CONSISTENT WITH THESE OBSERVATIONS, PRE-CLINICAL STUDIES FIND THAT MANY DRUGS USED IN THE TREATMENT OF GLomerULAR DISEASES REDUCE PROTEINURIA DUE TO DIRECT EFFECTS ON PODOCYTE FUNCTION AS OPPOSED TO IMMUNOMODULATION. THESE OBSERVATIONS SUGGEST THAT TREATMENT OF GLomerULAR DISEASES SHOULD INVOLVE THE BROAD CONCEPT OF COMBINING IMMUNOMODULATION THERAPIES WITH TREATMENTS DESIGNED TO STABILIZE PODOCYTE FUNCTION IN CONCERT WITH AGENTS THAT ARE ABLE TO PRESERVE PODOCYTE VIABILITY.

During this meeting, we will hear the lecture entitled ‘Glomerular disease and podocytopathies: Novel and evolving treatment regimens’, which will review evolving immunosuppressive and non-immunologic treatment for FSGS. The MENTOR trial is a ground-breaking trial comparing the complete or partial remission rates at 24 months in patients with idiopathic MGN who were randomized to either oral cyclosporin (CsA) or intravenous (IV) rituximab. In this study, IV rituximab was shown to not only be non-inferior to CsA in inducing complete or partial remission rates, it was also able to reduce the incidence of clinical relapse.

The concept of using combination drug therapy that modifies different cellular pathways in order to minimize toxicity has been increasingly used in the treatment of glomerular diseases. The DUET trial examined the efficacy of sparsentan (a selective antagonist of the endothelin alpha receptors) in combination with irbesartan therapy in patients with FSGS, and demonstrated an effective non-immunologic method for reducing proteinuria. Lastly, ACTH has been successfully used in combination with oral tacrolimus to induce complete or partial remissions in a group of multidrug-resistant FSGS and MGN patients. The growing therapeutic options for treating glomerular disease alone or in combination offers hope in the treatment of all forms of glomerular disease.[3]
Growing evidence for the role of water in the prevention of kidney pathologies

The latest scientific results will be presented at the Danone Nutricia Research symposium today.

Vasopressin, or the antidiuretic hormone, is a key player in total water body regulation by its action on the kidney in order to conserve water and concentrate urine via a well-described mechanism. Increasing water intake and/or reducing vasopressin secretion may have a beneficial effect on renal function in subjects with risk factors of developing various kidney pathologies. Between 8% and 10% of the adult population has a form of kidney damage and millions of people die of complications related to Chronic Kidney Disease (CKD).

Around 25% of adults are suffering from cardio-metabolic syndrome worldwide and almost 30% of women will experience at least one episode of cystitis during their life span. Considering the cost of health care, especially in low and middle income countries, and the increase of urapathogen resistance to broad-spectrum antibiotics, the best hope to reduce the human and economic cost of chronic pathologies lies in prevention. Thus, water appears as an affordable therapeutic recommendation to prevent kidney pathologies, decreases risk factor for cardio-metabolic disease and prevent urinary tract infection (UTI) recurrence.

Professor Louise Moist, MD, MSc from the University of Western Ontario (Canada), will bring a global vision on the recent advances in the scientific area of hydration and kidney health.

Dr. Sofia Enhörning, MD, PhD from Skåne University Hospital and Lund University (Sweden) will hold a lecture on plasma copeptin, a surrogate marker for vasopressin, as a predictor of cardiac-renal diseases using large population-based cohorts. “Previous studies in humans and animals suggest a role for vasopressin in renal function decline both in diabetes patients and in the general population. We recently discovered that elevated baseline copeptin was independently associated with increased risk of CKD development in two population-based Swedish cohorts – Malmö Preventive Project and Malmö Diet and Cancer Cardiovascular Cohort – followed for 9 and 20 years respectively.”

Dr. Mariacristina Vecchio, PharmD from Danone Nutricia Research (France) will describe the results of a prospective randomized controlled study investigating daily water intake in premenopausal women suffering from recurrent acute uncomplicated cystitis (rAUC). “As a preventive strategy, water is often recommended to women suffering from rAUC, however clinical data are lacking. The aim of this study was to evaluate the efficacy of increased daily water intake on the frequency of rAUC in premenopausal women.”

Professor William Clark, MD from the University of Western Ontario (Canada) will present for the first time the results of a randomized clinical trial increasing water intake in adults with CKD (n=533). About the safety of an increased hydration in CKD patients, Professor Clark says “increased hydration in CKD is both safe (no significant change in serum osmolality or sodium) without change in quality of life and effective in terms of increasing hydration”.

The Danone Nutricia Research symposium today is an opportunity to know more about the preventive role of water in cardio-renal diseases, UTI and CKD. Join us at 13h15 in Hall A3.

Friday, 15.00 – 16.30, Auditorium 10-11-12

Friday, 17.00 – 18.30, Hall A2

Lunch Symposium Danone Nutricia Research Friday, 13.15 – 14.45, Hall A3

To know more:

- 10th Hydration for Health Annual Scientific Conference, June 26th and 27th in Evian, France
- https://www.hydrationforhealth2018.com
- Twitter: @HH4Initiative

This article is sponsored by Danone Nutricia Research.

References


S 5.3
Uremic toxicity – New insights Friday, 15.00 – 16.30, Auditorium 10-11-12

S 5.7
Treatment of CKD-MBD Friday, 17.00 – 18.30, Hall A2

Fractures in kidney graft recipients

What’s the benefit of long-term anti-resorptive agents?

The risk for bone fractures is four-fold higher in patients with end-stage kidney disease compared with the general population, and increases further in the early post-transplant period. Kidney transplant recipients lose bone mass, particularly in the first year after transplantation, and are at increased risk for the development of osteoporosis and subsequent fractures. Older studies revealed a loss in bone mineral density (BMD) of up to 10% in the first year after transplantation.[1]

However, this loss in BMD appears to be less severe in the current transplantation era, because of changes over time in patient management, such as increased use of prophylaxis with calcium and vitamin D supplementation and lower doses of steroids. Despite this, prevention and/or treatment of osteoporosis post-transplant remains an important issue in the chronic management of kidney transplant recipients, since one in five patients may develop a fracture within five years after kidney transplantation. The risk factors for fractures include older age, female sex, diabetes, decreased versus living donor, steroid use and dosage, and use of proton pump inhibitors.[2]

The newest KDIGO guidelines for CKD-MBD[3] suggest that BMD testing be used in kidney transplant recipients to assess fracture risk if results will alter therapy, and that vitamin D deficiency and insufficiency be corrected using treatment strategies recommended for the general population. Furthermore, anti-resorptive agents such as bisphosphonates or the anti-RANKL antibody denosumab should be considered in the first 12 months after transplantation, whereas there is insufficient data to guide treatment after the first 12 months.

A recent meta-analysis of 12 studies evaluating the efficacy of bisphosphonates included 621 patients and described improvements in BMD of 6.0% at the femoral neck and 7.4% at the lumbar spine in patients taking versus those not taking bisphosphonate. However, this was not associated with a difference in fracture incidence between the groups.[4] Thus the use of bisphosphonates after kidney transplantation is associated with improvements in BMD but not with a reduction in risk for fracture.

In an open label, prospective, randomized trial of 90 patients we compared denosumab (two doses of 60mg at two weeks and six months after transplant) with no treatment.[5] At 12 months, lumbar spine BMD increased by 4.6% in the denosumab group and decreased by ~0.5% in the control group (between-group difference 5.1%); 95% CI, 3.1% to 7.0%; p < 0.001. Since this was a short study with a limited number of patients, the effect on fracture risk could not be evaluated.
ANCA-associated vasculitis in Japan Results from a nation-wide, prospective cohort study

Shinya Kaname & Kenji Sada
Okayama, Japan

The Research Committee on Intractable Vasculitides of the Ministry of Health, Labor and Welfare of Japan (MHLW) launched a nation-wide prospective ANCA-associated vasculitis (AAV) cohort study of remission induction therapy in Japanese patients with ANCA-associated vasculitides (RemIT-JAV). This study was followed by RemIT-JAV-RGN (Rapidly Progressive Glomerulonephritis), the cohort combined with that of the Research Committee on Intractable Renal Disease, giving a total registration number of 477 patients.

Of 159 patients enrolled in the RemIT-JAV cohort (2009 – 2010) cohort, 14 (9.0 %) were categorized with eosinophilic granulomatosis with polyangiitis (EGPA), 33 (21.2 %) with granulomatosis with polyangiitis (GPA), 78 (50.0 %) with microscopic polyangiitis and renal-limit ed vasculitis (MPA/RLV), and 31 (19.9 %) with unclassifiable vasculitis using the EMEA algorithm.

The average ages of EGPA (male/female, 5/9), GPA (12/21), and MPA/RLV (35/43) and unclassifiable were 63.6 %, 54.6 % and 45.5 % for GPA, 47.4 % for MPA/RLV, and 61.3 % for unclassifiable. The patients with ILD (n = 61) showed significantly lower BVAS, with fewer ear, nose and throat, and cardiovascular manifestations than patients without ILD (n = 95). The RemIT-JAV-RGN (2009 – 2010) cohort of 321 patients showed EGPA 9 %, GPA 17 %, MPA 62 %, unclassifiable 13 %, respectively, with more MPA/RLV patients than in the RemIT-JAV cohort. The remission rates were compared according to the three criteria for the severity of the diseases – the EUVAS-defined disease severity, the RGN clinical grading system in Japan, and the Five-Factor Score (FFS) – and we found no significant differences for remission rates in any of the three severity criteria. The Japanese RGN grading system was, however, more useful for predicting six-month overall and ESRD-free survival.

In conclusion, MPO-ANCA-positive MPA/RLV is the most common form of AAV in Japanese patients, and one half of patients with GPA were positive for MPO-ANCA. ILD is an important clinical manifestation in Japanese patients. In addition, the RPSN grading system was useful in predicting renal survival of AAV patients in Japan.

Complications after renal biopsy: what are the risk factors?: An analysis of Swedish registry data

Björn Peters
Skövde, Sweden

Percutaneous kidney biopsies have been performed since 1944 to establish diagnoses in the J-RBR registered from 2007 to 2017 will be summarized. Read the article of Hitoshi Sugiyama in our E-Issue.

Complications after renal biopsy: what are the risk factors?: An analysis of Swedish registry data

S 0.5 ERA-EDTA & Japanese Society of Nephrology Friday, 17.00 – 18.30, Auditorium 10-11-12

Japanese Renal Biopsy Registry

Hitoshi Sugiyama
Okayama, Japan

In this talk, the detailed data of the J-RBR and the frequencies of the clinical and pathological diagnoses in the J-RBR registered from 2007 to 2017 will be summarized. Read the article of Hitoshi Sugiyama in our E-Issue.

Complications after renal biopsy: what are the risk factors?: An analysis of Swedish registry data

S 0.5 ERA-EDTA & Japanese Society of Nephrology Friday, 17.00 – 18.30, Auditorium 10-11-12
Diabetic Kidney Disease: Exploring mechanisms and outcomes of SGLT2 inhibition

EBAC ACCREDITED SYMPOSIUM TO BE HELD DURING ERA EDTA 2018. COPENHAGEN, DENMARK

CHAIRMAN
Colin Baigent, MD
University of Oxford, United Kingdom

AGENDA
09:45 – 10:00
SGLT2 inhibition in Kidney Disease: What are the key lessons from the EMPA-REG OUTCOME trial?
Christoph Wanner, MD – University of Würzburg, Germany

10:00 – 10:20
Understanding CKD & SGLT2 inhibition: What are the key mechanisms for benefit?
Per-Henrik Groop, MD – Helsinki University and Helsinki University Hospital, Finland

10:20 – 10:40
Addressing the remaining questions on SGLT2 & CKD: A review of new outcome trials
Colin Baigent, MD – University of Oxford, United Kingdom

10:40 – 10:45
Discussion
All faculty

FRIDAY, MAY 25 2018, 09:45 – 10:45 HRS • MEETING ROOM C1-M0

n-3 PUFA and CKD: impact in the clinic?
The ORENTRA trial and other intervention studies

In order to design intervention studies with marine n-3 PUFA it is important to consider the kind of effects you will achieve depending on the dose of n-3 PUFA. Lower doses (from dietary intake) are sufficient for anti-inflammatory effects, while achieving, for example, an anti-inflammatory effect requires higher doses of at least 2.5 g daily. Inflammation is an important target for patients with CKD, since it promotes development of fibrosis and aging in both the heart and the kidney. It is well known that patients with CKD have insufficient intake of marine n-3 PUFA and subsequently low levels, which makes intervention in this patient group even more relevant.

Previous large intervention studies in cardiology have shown a significant effect from adding marine n-3 PUFA to standard of care, with a reduction in the rate of death and readmission for cardiovascular causes, in patients with heart failure. The OMEGA-REMODEL trial was a well-conducted randomized controlled trial (RCT) that included 358 patients who were assigned after myocardial infarction to either high-dose n-3 PUFA or placebo. After six months of intervention the patients treated with n-3 PUFA had better left-ventricular systolic volume index, less fibrosis (evaluated with MRI) and better ejection fraction. This is the first major study to show an effect from n-3 PUFA on development of fibrosis in a clinical setting. Data on kidney function/fibrosis are more sparse. The ALPHA-Omega trial was a large RCT in patients post-myocardial infarction. Patients were randomized in four arms to different kinds of low-dose fatty acids and followed for 40 months. Investigators found that in the group treated with n-3 PUFA there was less decline in renal function measured by eGFR. Some studies in IgA-nephrop-this have also shown that high-dose n-3 PUFA may halt decline in kidney function and reverse proteinuria, although data in this field are conflicting.

In this lecture we will present new, unpublished data from the ORENTRA trial, which was a RCT in renal transplant recipients (RTRs). Patients were randomized to either 2.6 g of n-3 PUFA or placebo eight weeks after transplantation and followed for 44 weeks.

The primary endpoint was mGFR and secondary endpoints were inflammation and fibrosis in the graft evaluated with several methods. Results from this trial will be presented, as well as the protocol for a larger ongoing trial with n-3 PUFA in RTRs, EMIRA.

S 4.7
n-3 PUFA in CKD: does it matter?
Friday, 17.00 – 18.30, Auditorium 15

References
03. Elde 1A, Reinhold FF, Jenssen T, et al. Marine n-3 fatty acid supplementation prevents increase in graft fibrosis after renal transplan- tation: a randomized controlled trial. Manuscript submitted for publication.

S 0.5
ERA-EDTA & Japanese Society of Nephrology Friday, 17.00 – 18.30, Auditorium 10-11-12

References
01. Peters B (2016). Clinical and quality aspects of native and transplant kidney biopsies in Sweden. Both these registries together contain data from more than 2,800 native kidney biopsies. The analysis of the data is ongoing and the results will be presented during the Symposium "Acute/rapidly-progressive nephritic syndrome and vasculitis (organized jointly by ERA-EDTA & JSN – Japanese Society of Nephrology) on 25th May 2018 at 17:00 – 18.30.
n-3 polyunsaturated fatty acids (PUFAs) are essential fatty acids that cannot be synthesized by humans, but are necessary for survival and must be consumed in the diet. Seafood, especially fatty fish and fatty fish oils, together with oils from certain nuts and plants, are the major sources of n-3 PUFAs.

After ingestion, n-3 PUFAs are incorporated into the phospholipid layer of cell membranes, and are released into the cytoplasm by enzymatic action as free n-3 PUFAs. They then enter the nucleus where they upregulate the expression of anti-inflammatory and lipid-oxidizing genes. In addition, n-3 PUFAs enter the circulation where they competitively inhibit arachidonic acid, leading to production of cytokines with low inflammatory properties.

The beneficial effects of n-3 PUFAs were first discovered by Jørn Dyerberg, Hans Olaf Bang and Aase Nielsen during their expedition across Greenland, where they found higher serum n-3 PUFAs levels and lower serum cholesterol in Eskimos compared to the average Danish control population. Gas chromatography was the method then used for n-3 PUFAs analysis and is still the gold standard.

Epidemiological studies provide support for n-3 PUFAs’ protective effect against heart disease by beneficially influencing risk factors like dyslipidemia, inflammation and high blood pressure. Patients with chronic kidney disease (CKD) are at high risk of cardiovascular disease (CVD). In addition to positive effects on traditional risk factors for CVD, studies have shown possible membrane-modifying and anti-arrhythmic effect by n-3 PUFAs in CKD.

Prospective cohort studies have demonstrated an inverse association between plasma n-3 PUFAs levels and the decline in renal function that commonly occurs with aging. Similar findings have been found in patients with type 2 diabetes mellitus, in whom high levels of n-3 PUFAs in red blood cells were associated with less renal function decline in relation to inflammation.

The most common cause of death in hemodialysis patients is sudden cardiac death (SCD), with the risk of dying highest in the first few months after starting treatment. In a case-control study, higher levels of n-3 PUFAs were associated with reduced risk of SCD in hemodialysis patients. In addition, cohort studies have shown inverse associations between levels of n-3 PUFAs and all-cause mortality. This might be important, as previous studies have shown that patients on hemodialysis generally have lower levels of n-3 PUFAs, compared to not only healthy individuals, but also other patient populations. Epidemiological studies on renal transplant recipients (RTRs) and n-3 PUFAs show promising results. In an observational study including 1,990 RTRs, n-3 PUFAs levels were positively associated with better patient and graft survival. In addition, the rate of late rejection (defined as rejection three months after transplantation) was lower in the presence of high levels of n-3 PUFAs.

Findings from these studies suggest that n-3 PUFAs may be important in several settings of kidney disease.

Get The Most Out Of ERA-EDTA 2018
Complete 10 digital learning activities and get an ENP T-Shirt for free

Get ready for more learning and discoveries and be rewarded not only with new knowledge but also a fashionable ENP T-Shirt.

Collect stamps on your personal Flyer for completing digital learning activities like the Knowledge Test, a visit to the E-poster Gallery, finding out more about Rare Diseases, accessing Speaker Presentations on ENP, participating in Live Voting etc.

For more information about your personal quest check your Flyer or visit the ENP station at the e-campus in Hall E.
SESSIONS

09:45 Welcome and introduction
Professor Thomas Benzing, Germany

09:50 The ERA-EDTA guidelines in clinical practice
Dr Roser Torra, Spain

10:05 Identifying patients with ADPKD at risk of worsening renal function – the GERMAN Experience
Dr Roman-Ulrich Müller, Germany

10:20 Clinical scenarios – a practical approach
Professor Yannick Le Meur, France

10:35 Questions, summary and close
Panel Discussion led by Professor Thomas Benzing, Germany

**Dear Colleague**

It is my great pleasure, as Chair, to invite you to join us for the symposium ‘Up to Speed with Rapid Disease Progression in ADPKD’.

Our Faculty of expert clinicians will lead us through a programme reflecting on the identification and management of rapid progression in patients with ADPKD. They will share their personal experience of the practical application of the ERA-EDTA guidelines on ADPKD and their real-world experience of managing challenging cases through interactive clinical scenarios.

Your Faculty for this event who will lead us through this engaging programme are:

- **Dr Roser Torra**, Nephrology Department, Puigvert Foundation, Barcelona, Spain
- **Dr Roman-Ulrich Müller**, Renal Unit, University Hospital Cologne, Germany
- **Professor Yannick Le Meur**, CHU La Cavale Blanche, Brest, France

We look forward to seeing you there.

**Professor Thomas Benzing**
Department II of Internal Medicine,
University of Cologne, Germany

---

**Saturday 26th May 2018, 09:45-10:45**
Room C1-M4, Bella Center, Copenhagen
The Japan Renal Biopsy Registry (J-RBR) was started in 2007, followed in 2009 by the initiation of the Japan Kidney Disease Registry (J-KDR) by the Committee for the Standardization of the Renal Pathological Diagnosis and the Committee for the Kidney Disease Registry of the Japanese Society of Nephrology. Appointed clinical training hospitals of the JSN and the Japanese Society for Dialysis Therapy were asked to participate in the J-KDR, including the J-RBR, in an attempt to extend the registry nationwide.

By the end of 2017, data from 40,369 cases were registered, and 144 facilities were participating. The most common clinical diagnosis in 2007–2017 was chronic nephritic syndrome (51.8%), followed by nephrotic syndrome (24.2%) and rapidly progressive nephritic syndrome (6.6%). Acute nephritic syndrome was separately categorized in J-RBR, accounting for 1.9% of cases. The most frequent pathological diagnosis from 2007 to 2017 in the J-RBR was IgA nephropathy (IgAN), accounting for about 30% of cases.

In the category of rapidly progressive nephritic syndrome, more than half of cases were ANCA-positive nephritis (54.5%), with MPO-ANCA nephritis accounting for 51.8% and PR3-ANCA nephritis for 2.7%. Anti-GBM nephritis accounted for 5.0% followed by IgA vasculitis at 2.1%. Regarding the pathological diagnosis, crescentic and necrotizing glomerulonephritis (GN) was predominant (63.4%) followed by mesangial proliferative GN (7.3%). Patients with ANCA-negative crescentic GN exhibited proteinuria significantly more frequently than those with ANCA-positive nephritis.

Japanese studies from 1988 to 2007 showed that, in patients with ANCA-associated vasculitis exhibiting rapidly progressive nephritic syndrome, the one- and five-year survival rates were 78.4% and 62.0%, respectively. Among the patients registered in the past five years, the patient survival rate was slightly improved, but there was no marked improvement in renal survival. Maintenance treatment avoiding relapse should be established to improve the renal outcomes.

In this talk, the detailed data of the J-RBR and the frequencies of the clinical and pathological diagnoses in the J-RBR registered from 2007 to 2017 will be summarized. The characteristics of acute/rapidly-progressive nephritic syndrome in Japan will be presented.

**References**


Large-scale genomic studies: what have we learned? New insights into the physiology of kidney function and kidney disease

During the last decade, huge efforts were undertaken to search for genetic risk factors underlying common traits and diseases. Genome-wide association studies (GWAS) revealed thousands of genetic associations predominantly based on single nucleotide polymorphisms (SNPs), including more than 60 common SNPs related to kidney function. Large collaborative consortia like the OGD-Gen Consortium, embedding multiple studies around the world, were created to conduct this unbiased research using an agnostic approach.

Although the findings were replicated and robust, the effect sizes of these associations were often quite small, and thus their direct clinical relevance might be questioned. However, they provided insight into biological pathways that help us to understand the physiology of kidney function and kidney disease. Furthermore, it turned out that some of these kidney-related genes discovered in population-based GWAS substantially increased the risk of severe kidney disease.

Initial studies focusing on rare variant associations in population-based samples indicated that large sample sizes are required to reveal such association with kidney function, and this will be a task for the future. Finally, these large-scale GWAS association results provide a basis for conducting Mendelian randomization studies by using SNPs as instruments to infer causality of various traits on kidney function or disease, or vice versa.

Prediabetes and insulin resistance in patients on the waiting list

Post-transplant diabetes mellitus (PTDM) is a common complication after renal transplantation and is an established risk factor for cardiovascular disease and mortality. Recognition of modifiable risk factors for PTDM while patients are on the waiting list (WL) enables intervention, as well as planning of the immunosuppression at renal transplantation. We performed an oral glucose tolerance test (OGTT) in 155 non-diabetic, wait-listed patients. Baseline, 30mn and 120mn glucose and insulin levels were measured and insulin sensitivity (IS), first-phase insulin secretion (InSecr), and disposition index (DI: the product of measures of IS and InSecr) calculated. We detected unmasked diabetes in 8% and glucose intolerance in 20% of patients, while 72% were euglycemic. Patients with an abnormal OGTT exhibited a decreased IS and DI, which resulted in a reduced capacity to compensate for insulin resistance. In addition, they were older, and had higher body mass index (BMI), triglycerides and HbA1c levels. In the second part of the study we prospectively followed 71 patients with a functioning graft one year after transplantation. PTDM developed in 29% of the patients. Pretransplant IS was lower and age, BMI, 120mn glycemia and HbA1c were higher in those patients destined to develop PTDM. A BMI ≥ 28 kg/m² or HbA1c ≥ 5.3 had the best predictive value for PTDM. In conclusion, an abnormal OGTT is not uncommon in wait-listed ‘non-diabetic’ patients, and the underpinning pathophysiology is a reduced capacity to compensate for an increased insulin resistance. This imbalance facilitates the development of PTDM after exposure to immunosuppression. Finally, pretransplant BMI and HbA1c are acceptable predictors of PTDM.

The age-old problem in nephrology Delivering holistic care to an aging CKD population

Increasing numbers of incident and prevalent patients cared for by renal services in first world countries are elderly or very elderly. Indeed, in my unit the oldest dialysis patient reached the remarkable age of 105 late last year. For many, the travel and other treatment burdens are unbearable. Meantime, physicians whose specialty is elderly care medicine are learning to work in multidisciplinary teams and to cross hospital and community boundaries to deliver holistic care to our aging population. There is much-needed emphasis in many countries on advanced care planning for end of life.

In my lecture, I will consider the questions raised by our aging patient population in nephrology. I will ask how we can deliver the best possible care to these folks and what lessons we can learn from our geriatrician colleagues. I will explore the concept of maximinum conservative management (MCM) for stage 5 CKD as practiced in my unit for over a decade. Similar models of care have many labels, including renal palliative or renal supportive care. There has been a lot of debate around what it means for patients in reality; a UK study suggests that practices differ widely. I will rehearse the nuances around these different terms and how and why these services vary. I will look at the historical context and practical application of MCM. I will examine the evidence surrounding benefit and harm when treating elderly folks with advanced CKD. I will review what is known about survival when comparing conservative with dialysis therapies. I will also consider the influences of cognitive function in decision making, the effects of dementia and delirium and the role of family and close personal support.

I will share the experiences we have had in the UK when grappling with these issues. Finally, I will introduce the recently initiated UK National Institute for Health Research-funded randomized controlled trial called ‘Prepare For Kidney Care’, which is centered on elderly or highly comorbid patients with stage 5 CKD, where there is uncertainty about the best treatment options. The randomization is to either preparation for dialysis according to the standard practices of the unit or to a more holistic approach, where priorities of care are discussed and hospital visits minimized or conducted in the patient’s home and attention paid to advanced care planning.
Tailor treatment to each AAV patient
Clinical trials and improving survival in ANCA-associated vasculitis

During the last 10–15 years there have been better patient outcomes in antineutrophil cytoplasm antibody (ANCA)-associated vasculitides (AAV). This is due in part to several trials that were launched to evaluate and reduce the toxicity of drugs used in the immunosuppressive treatment of this chronic and relapsing disease entity.

The randomized controlled trials (RCT) performed by the European Vasculitis Study Group (EUVAS) have raised awareness of adverse events due to drug toxicity. Current treatment has therefore been organized into more aggressive induction of remission to rapidly halt disease activity and maintain remission in order to diminish long-term vasculitis-provoked organ damage. There is a direct correlation between minimizing the intensity of therapy and the clinical situation. New, less toxic treatment and reduction of total immunosuppressive exposure during the induction of remission have improved patient outcomes especially in patients with renal failure.

During this induction phase, infections contribute more to the negative outcome than active vasculitis (Little 2009). Older AAV patients and patients with low eGFR are most susceptible to infections and infection-related mortality with eGFR as the most important predictor. Patients who present with severe renal disease have an increased risk of developing more severe adverse events. This is probably related to lower excretion of active drug metabolites and the influence of uremia on immunodefense.

The use of cotrimoxazole as Pneumocystis jiroveci pneumonia (PCP) prophylaxis during cyclophosphamide (CYC) and rituximab (RTX) treatment has lowered the incidence of PCP infection-related treatment failure. However, up to 30% of patients on RTX have been shown to develop hyponagammaglobulinemia, which contributes to infections. Thus, the efficacy of RTX as an alternative to CYC in order to reduce infections/adverse effects has not been yet established. RTX is more frequently used in younger patients because of the effect of CYC on male fertility. Sperm samples should be stored before CYC treatment is initiated.

The long-term outcome of AAV is influenced by diabetes, malignancies, osteoporosis and cardiovascular adverse events, mostly related to corticosteroids (GCS). Relevant prophylactic measures against GCS organ damage are necessary. Lowering GCS exposure reduces side effects, but the risk of relapses has been reported as increased (Walsh) or unchanged (McGregor). Longer GCS treatment could improve patient outcome but has more side effects. The use of methylprednisolone pulse (MP) at treatment initiation has never been proved effective in an RCT and a retrospective study showed a higher frequency of infections and diabetes without better renal outcome (Chanouzas).

New, less toxic drug regimens have already been proposed, combining plasma exchange (PLEX) and low-dose CYC (Szpirer) or low dose CYC and RTX (McAdoo). The results of the PEDIVAS RCT, in which +/- PLEX, CYC or RTX were used with standard/reduced dose of GCS during induction, will be presented during this Congress. CLEAR, another RCT, showed the positive effect of using CYC/RTX together with a CsA inhibitor (avacopan) for induction as a possible agent that can be used with reduced/or instead of GCS. The upcoming CsA inhibitor study Advocate will hopefully answer this question.

The severity of renal AAV cases can be classified based on kidney biopsy results and treatment response or failure predicted on chronicity findings. The unchanged presence of proteinuria at 12 months predicts worse long-term outcome (Szpirer) and should be addressed. Patient quality of life should be monitored using patient surveys (SF36/EQ-5D), and is as important for long-term follow-up evaluation as successful renal therapy. Chronic fatigue has been reported as a significant factor in patient wellbeing. The additional disease management procedures should then be considered in AAV treatment.

Regular follow-up schedules similar to those used in kidney transplant patients are recommended for monitoring bone marrow suppression during induction, and possible relapses during maintenance therapy – especially in patients with granulomatous with polyangiitis. Tailoring each treatment individually, based on phenotype, age, and renal deterioration, would be the ideal solution to improve prognosis. EULAR/ERA-EDTA guidelines can be effective tools in treatment planning and execution.

Reducing death risk on dialysis
Arrhythmias and sudden cardiac death in dialysis patients: is n-3 PUFA of relevance?

One of the main challenges in the management of patients with end-stage renal disease (ESRD) is cardiovascular disease. It is the leading cause of death, and sudden cardiac death (SCD) is responsible for almost 30% of all deaths in ESRD patients. The mechanisms behind the increased risk of SCD are complex and not fully understood, making preventive measures difficult.

In the general population, SCD is frequently a result of malignant ventricular arrhythmias, but the arrhythmias preceding SCD in patients with ESRD are less well described. Some studies indicate that ventricular arrhythmias are most important, but other studies on cardiac arrest in dialysis units and small clinical studies with data from implantable loop recorders suggest that bradycardia, asystole and pulseless electrical activity as a cause of SCD may be more common than in the general population. However, it is unclear whether bradycardiac SCD are the result of another fatal event or an underlying conduction system disease. Ventricular and atrial arrhythmias are more common during and immediately after the dialysis session. Furthermore, there is an increased risk of SCD in the peridialytic period, especially linked to the first dialysis of the week after the longest interdialytic interval. The nature of the arrhythmias linked to SCD thus might differ in different settings, depending on the individual patient and whether they occur during dialysis or in the patient’s home.

New initiatives to reduce the risk of SCD are warranted, and n-3 polyunsaturated fatty acids (PUFA) derived from fish might be of importance. Marine n-3 PUFA have several positive effects on cardiovascular health. Studies have shown antiarrhythmic effects and effects on autonomic modulation of the heart, and a number of large randomized controlled trials (RCT) reported that marine n-3 PUFA reduced major cardiovascular events in the general population. The American Heart Association recommends supplements of marine n-3 PUFA as a reasonable treatment in the secondary prevention of coronary heart disease and heart failure.

Currently, there is no formal recommendation on intake of marine n-3 PUFA in patients with ESRD due to the lack of evidence in this population. Epidemiologic studies suggest a lower mortality in dialysis patients with a higher intake of marine n-3 PUFA. Only one RCT by Svensson and colleagues has investigated effects on major cardiovascular endpoints, and this showed no effect of marine n-3 PUFA on a composite primary endpoint of total cardiovascular events and death in 206 hemodialysis patients with known coronary heart disease. However, they observed a significant reduction in myocardial infarction as a secondary outcome. Effects of marine n-3 PUFA on cardiac autonomic function and arrhythmias in patients with ESRD are uncertain and have only been addressed in a few small studies, but new evidence is in the pipeline.

Patients with ESRD in the Western world have a low intake of marine n-3 PUFA with low levels in the blood. This could be corrected by supplements, but should we use marine n-3 PUFA as part of the treatment of these patients with the current level of evidence?
n-3 PUFA and chronic kidney disease
Interventional studies relevant for the nephrologist

IVAR ANDERS EIDE
Oslo, Norway

n-3 PUFA in chronic kidney disease (CKD) – does it matter? You might think that if marine n-3 PUFAs really were beneficial for health, five decades of clinical trials would have produced clear evidence for this hypothesis, that there would be no more secrets to reveal and that we would all be taking fish-oil supplements. If so, I recommend you to attend this lecture, where we make four stops on the marine n-3 PUFA renoprotection line. At each stop, we will explore established and proposed marine n-3 PUFA anti-inflammatory and anti-fibrotic effects that may halt decline in renal function in patients with CKD.

The first stop is inflammation. Several mechanisms by which marine n-3 PUFA may prevent inflammation have been reported, including competitive inhibition of arachidonic acid as substrate in prostaglandin and leukotriene synthesis, tumor necrosis factor pathway inhibition and reduced adhesion molecule expression.[1] In this lecture, we will take a look at clinical trials that either investigated renal tissue cytokine levels or determined degree of inflammation in the renal cortex by light microscopy after marine n-3 PUFA supplementation.

The next stop is peroxisome proliferator activated receptor (PPAR) agonism. Marine n-3 PUFAs serve as endogenous ligands for PPARs, where they act as agonists. PPAR alpha and gamma activation may reduce inflammation and halt or even reverse fibrosis, partly through inhibition of nuclear factor kappa-B pathway. I will present data on the degree of interstitial fibrosis after marine n-3 PUFA supplementation from a recent clinical trial.

We then stop at protectins and resolvins. Marine n-3 PUFAs are precursors to these potent inflammation-resolving mediators. At this stop I will present some of the fascinating work by Professor Serhan on this topic.[2]

The last stop before we reach renoprotection is cellular senescence (CS). Cells subject to oxidative stress will reach their capacity for dividing prematurely and go into a senescent state of irreversible growth arrest, instead of being cleared by the immune system. CS might be induced through the p53-p21 pathway or the p16INK4a pathway, and is linked to development of fibrosis. The role of marine n-3 PUFAs in the prevention of CS is unclear. Promising results after marine n-3 PUFA supplementation on expression of p16INK4a and telomere shortening suggest that marine n-3 PUFAs may halt premature aging.

Proposed and established biological effects of marine n-3 PUFAs indicate that several inflammatory and fibrotic pathways might be altered. However, as pointed out in the previous lecture by Professor Svensson, dose matters, and it is rarely clinically meaningful to provide patients with doses typical of a Western diet. The effects of marine n-3 PUFA supplementation are still scarcely studied in CKD. If high intake of marine n-3 PUFAs really is renoprotective, then the answer is our question should be yes: n-3 PUFA in CKD – it does matter.

References


New ideas on the link between salt and hypertension

FRIEDRICH C. LUFT
Berlin, Germany

Hypertension is a complex trait determined by both genetic and environmental factors. Among environmental factors, dietary salt intake is regarded as the most common and important risk factor for hypertension. However, blood pressure responses to dietary salt intake vary considerably among individuals, a phenomenon known as salt sensitivity of blood pressure. More than 50 years ago, Guyton and colleagues introduced the idea that the kidney is central to salt regulation, particularly concerning the regulation of renal pressure natriuresis. They proposed that a high-salt diet engenders sodium accumulation, volume expansion, cardiac output adjustments, and autoregulation for flow maintenance. The autoregulation in all vascular beds increases systemic vascular resistance, causing the kidneys to excrete more salt and water, thus reducing systems to normal and minimizing any changes in blood pressure.

More recently, Kuret et al. have challenged the idea that increased sodium reabsorption, salt retention, transient increases in cardiac output and subsequent autoregulation are responsible for salt-sensitive increases in blood pressure. They argue that the ability of individuals to respond with an appropriate vasodilatory response to increased salt intake is pivotal, in that the gene defects underlying Mendelian, salt-dependent hypertension could be related to subnormal vasodilatory responses to salt and could involve mechanisms outside the kidneys.

We have identified a Mendelian form of hypertension that is unrelated to sodium reabsorption in the distal nephron, and develops because of increased systemic vascular resistance. In addition, as a result of long-term balance studies conducted in simulation flights to Mars, we have discovered a third salt-storage compartment, which is situated largely in the skin. This compartment operates independently of renal function, and involves sodium binding to proteoglycans, a common connective tissue molecule. When disturbed, the skin compartment is associated with salt sensitivity, and is regulated by immune cells capable of detecting very local differences in sodium concentrations not reflected by the plasma concentration. More recently, we found novel molecular mechanisms demonstrating how the kidneys excrete large salt quantities with minimal water loss, which may be relevant to regulation of blood pressure in the presence of varying salt intakes.

The underlying mechanisms that promote salt sensitivity are clearly complex, but salt appears to be stored in the body as a three-compartment (or more) model, rather than the traditional two-compartment model. We are currently testing the hypothesis that water conservation within the renal concentration mechanism is a better indicator of the relationship between a high salt diet and blood pressure by analyzing twice-daily blood pressure measurements at three different levels of salt intake – 6 g/d, 9 g/d, and 12 g/d – corresponding largely to recommended guidelines, epidemiologic findings, and presumed current American and Western European dietary intake, respectively.

References


S.4.8 n-3 PUFA in CKD: does it matter?
Friday, 17.00–18.30, Auditorium 15

S.8.2 A new life for sodium in Nephrology
Friday, 15.00–16.30, C1-M1-2
The 55th Congress Organising Committee is very pleased to invite you to the Run for Kidneys 2018 which will take place on May 25, 2018 at 16:00 during the Copenhagen Congress.

The Start and Finish area will be located at Amager Fælled, very close to the Bella Sky Hotel.

The price for the race is DKK 149 (20 euro) + DKK 20 (2.5 euro) fee. The price will be charged in Danish Krone. Your participant fee will be donated by ERA-EDTA to the charity organisation "Læger uden Grænser"/Medicines sans Frontiers.

The Run for Kidneys Desk is available for online registrations confirmation, onsite registrations and any information related to the Run. The Run for Kidneys Desk is located in the Auditorium Foyer, Bella Center Ground Floor.
SHINE THE LIGHT ON NEW WAYS OF TREATING YOUR PATIENTS

PD THERAPY with SHARESOURCE
A new direct, 2-way connection that gives you an advanced way to treat home patients and maximize clinical efficiency.

HDx THERAPY enabled by THERANOVA
An expanded hemodialysis therapy that opens up a new option for patients requiring hemodialysis.

SYMPOSIA
Join us to learn about both of these therapies in practice and what this can bring to your patients. Attend our symposia to find out more!

A WORLD OF POSSIBILITY AWAITS
Visit our booth for a unique experience that explores how the light to saving and sustaining lives shines strongest when we all work together.

VISIT US TO DISCOVER MORE!
BOOTH 3.161

Baxter, Sharesource and Theranova are trademarks of Baxter International Inc. or its subsidiaries.

hdxtheranova.com