country involved to make European nephrology stronger!

eration of “leaders in nephrology”, who I am sure will maintain and nourish our discipline, even fight for it. This is something we have been doing for quite a while, too. In a way, nephrology is a threatened specialty and we took strategic steps to strengthen it. To achieve that, it is important to combine forces, so we established partnerships with the other main kidney associations, namely the International Society of Nephrology (ISN) and the American Society of Nephrology (ASN). This collaboration was officially declared during the Welcome Ceremony at our Congress in Vienna last year, at the ASN Congress in Chicago and at the WCN in Mexico. We have launched various joint projects, for example on the burden of kidney disease, on ethical issues in nephrology and on a survey based on the nephrology workforce.

Is this also the reason why ERA-EDTA has intensified its collaboration with the national societies of nephrology?

Yes, it is, and I would like to emphasize that I am very satisfied with this new and dynamic collaboration with the national societies. We have the National Village at the Congress and we are organizing annual meetings, where we share ideas and inform each other about promising national activities and projects that add to nephrology’s importance. To intensify the collaboration, we have created the “ERA-EDTA Activation Committees”. There are currently three of them – for Northern, Southern and Central European countries. The idea was to actively involve those countries that have had no representatives on the ERA-EDTA Council, in Working Groups or in
Our aim is to get every country involved to make European nephrology stronger!

Interview with the ERA-EDTA President, Professor Andrzej Więcek

Professor Więcek, your term as ERA-EDTA President will end after this Congress. Are you happy with how the ERA-EDTA has developed?

Yes, of course I am very happy to see the continuous growth of the ERA-EDTA – not only in terms of membership, but also in the form of many new initiatives it has launched. For that I would like to express my sincerest thanks and gratitude to all the ERA-EDTA Council members, especially the main officers (Secretary-Treasurer: Prof. Jonathan Fox and Chairperson of the Administrative Offices: Prof. Markus Kettrler), and also to the persons who work at our headquarters in Parma (especially Miss Monica Fontana, Ms. Silvia Argiolas and Mr. Paolo Zavalloni) for their enthusiasm and very effective work. ERA-EDTA's mission is to improve education in nephrology and to establish better treatment of patients. We have all been working hard together to achieve this, and I think we have made a lot of progress.

Which milestones have been reached during your presidency?

Well, we started many new initiatives and projects in order to strengthen our discipline. It is impossible to mention all of them, so I will give just a few examples. Some years ago, I promoted, even pushed for the establishment and development of the Young Nephrologists' Platform (YNP). Now I am really proud when I see this committee has evolved. It has started various new projects and its board members are very active. They have already organized several CME courses and advisory programs. Collaboration with the ASN has now been started, which is great, because networking means a lot in our modern world. The YNP has become a real success story and a role model for other nephrology associations, not only in Europe. When we created the YNP, one aim was to encourage young doctors to become nephrologists, and I have the feeling that many younger colleagues are attracted to nephrology and to the ERA-EDTA because of it. It is also nice to see the growth of the next generation of "leaders in nephrology", who I am sure will maintain and nourish our discipline, even fight for it. This is something we have been doing for quite a while, too. In a way, nephrology is a threatened specialty and we took strategic steps to strengthen it. To achieve that it is important to combine forces, so we established partnerships with the other main kidney associations, namely the International Society of Nephrology (ISN) and the American Society of Nephrology (ASN). This collaboration was officially declared during the Welcome Ceremony at our Congress in Vienna last year, at the ASN Congress in Chicago and at the WCN in Mexico. We have launched various joint projects, for example on the burden of kidney disease, on ethical issues in nephrology and on a survey based on the nephrology workforce.

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Opening ceremony

Nephrology has always been, and will continue to be, an innovative, exciting and pioneering specialty that is moving forward to improve the lives of people with chronic kidney disease. This was the message for delegates from Professor Jorge B. Cannata-Andia, Congress President, and Professor Andrzej Więcek, ERA-EDTA President, at yesterday’s Opening Ceremony of the 54th ERA-EDTA Congress. In celebration of nephrology's record of innovation, the ERA-EDTA Awards were presented to four nephrologists who have all made outstanding contributions over many years of achievement: The Award for Outstanding Basic Science Contributions to Nephrology to Professor Dotschas Kjerjaschki, the Award for Outstanding Clinical Contributions to Nephrology to Professor Giuseppe Remuzzi, the Award for Outstanding Educational Contributions to Nephrology to Professor Peter Stenmark, and the Award for Outstanding Contributions to ERA-EDTA to Professor Jonathan G. Fox. Doctor Albertien van Eerde received the Stanley Shaldon Award for Young Investigators, and Professor François Berthou was awarded with ERA-EDTA Honorary Membership. Finally, delegates had a glimpse of nephrology's exciting future with a fascinating lecture on 'New approaches towards kidney regeneration' by Professor Juan Carlos Izpisua Belmonte, La Jolla, USA.
other ERA-EDTA organs over the past five years. We want to address these countries and find out about their needs and expectations. Our aim is to get every country involved to make European nephrology stronger.

But let’s be honest, can a medical society like the ERA-EDTA really enhance the significance of nephrology? Yes, it can, and ERA-EDTA has achieved that. It promotes scientific projects and interdisciplinary ventures and gives financial support to young colleagues. In this way, ERA-EDTA plays its part in the way for innovations and independent science.

During my term, the activities of the ERA-EDTA Working Groups were intensified. They organize their own CMES and publish many papers. This is something I am very proud of. The same with the ERA-EDTA Registry. Very recently, it published a paper in “The Lancet” in collaboration with the Pediatric Registry – an indication of its high level of scientific quality, and acquired an EU Grant within the framework of the EDDH project. Not to forget the activities of ERBP, that during my term produced several new guidelines and position papers which now form the international standards for treating kidney patients. In addition, there are our Congresses. There is no doubt that the scientific level of the ERA-EDTA Congresses has greatly increased, as was shown in a survey we conducted last year. Mention must also be made of ours journals. For the first time in its history, NDT now has an impact factor greater than one. Cardiovascular disease (CVD) is the leading cause of death in CKD patients. Cardiovascular abnormalities (i.e., arterial stiffness, vascular dysfunction, and sudden cardiac death).

The three years went quickly and I enjoyed them very much. They were one of the best periods in my life. At this point, I would like to express my gratitude to all ERA-EDTA members for their confidence and trust in me. I will always be proud that I had the opportunity to be president of such an innovative and excellent medical association.

What will I miss? Well, I will certainly receive fewer emails [laughs]. On top of that, I will probably travel abroad less. In my role as ERA-EDTA President I used to be invited by many national societies of nephrology to their national congresses, and I travelled to the ISN and ASN congresses, and attended various ERA-EDTA meet- ings throughout Europe. I always enjoyed these meetings and tried to accept every invitation in order to make ERA-EDTA known more widely. This was very interesting and fulfilling, but at the same time very time-consuming. I will certainly miss the work I have been doing in recent years – but I’ll have more time for patients in my department and also for my family. [cla]

Uremic toxins: a cause of cardiovascular disease in CKD?

The uremic syndrome is a complex condition of numerous organ dysfunctions. It is attributed to the retention of a myriad of compounds that under normal conditions are excreted by the healthy kidneys, and that are currently called uremic toxins (Figure). These toxins can be subdivided into a family of three groups of molecules:

1. Small, water-soluble molecules
2. So-called ‘middle molecules’ and
3. Protein-bound molecules.

Most of them have been shown to be associated to different extents with one or more complications of chronic kidney disease (CKD). Many of these uremic toxins contribute particularly to the development of cardiac disease in these patients. Cardiovascular disease (CVD) is the leading cause of death in CKD patients, with a steadily increasing risk as kidney function declines. The risk is up to 10–20 times higher in end-stage kidney disease (ESKD) than in the general population. CKD is mainly associated with two types of CVD: accelerated atherosclerosis and more specifically CKD-related pathologies, including arteriosclerosis, vascular calcification, and cardiac abnormalities (i.e. uremic cardiomyopathy, diastolic dysfunction, and sudden cardiac death).

Numerous experimental studies have shown that the accumulation of phosphate in advanced stages of CKD induces cardiovascular abnormalities, either directly or indirectly via, for instance, an increase in serum PTH and/or fibroblast growth factor 23 (FGF23) and a decrease in Klotho. Moreover, many in vitro and in vivo studies have highlighted deleterious effects of elevated extra-

Further studies are needed to prove that reducing uremic toxins lowers cardiac risk

in chronic hemodialysis patients. Finally, several observational and experimental studies have demonstrated an association of excessive serum levels of the uremic toxin indoxyl-sulphate with abnormalities of the cardiovascular system in CKD.

These observations favor experimental and clinical attempts aimed at improving patient outcomes by reducing high circulating levels of uremic toxins. However, although supported by several post hoc analyses, the different clinical approaches chosen have to date been insufficiently powerful to reach this goal. In conclusion, uremic toxins play a central role in the crosstalk between the diseased kidney and cardiac disease of CKD. Further studies are needed to prove the hypothesis of a causal relationship, with convincing therapeutic consequences. [cla]

Session 15
Heart failure in chronic kidney disease
Sunday, 15.15 – 16.45, Hall H103 – 104
Prof. Remuzzi has coordinated the Negri Bergamo laboratories of theMario Negri Institute for Pharmacological Research and the affiliated Ado e Cie Daccio Clinical Research Center for Rare Diseases in Ranica, which comprises a group of basic scientists, physiologists, pharmacologists, molecular and cellular biologists, pathologists and clinicians devoted to the study of human renal diseases and their corresponding animal models from the perspective of pathophysiology and therapeutic intervention. He has been involved in major advances in many areas of nephrology for example new insights into many disorders, including the interactions between plasminogen and endothelium, the pathophysiology of glomerular diseases and the factors that influence the progressive loss of kidney function. His work has focused on improving the outlook for patients with end stage renal disease. Prof. Remuzzi has served and still serves in editorial boards of many journals: The Lancet, New England Journal of Medicine, American Journal of Kidney Diseases, Nephrology Dialysis Transplantation, Journal of Nephrology, Kidney International, International Yearbook of Nephrology, Nephron, Kidney, Journal of the American Society of Nephrology and many others. Prof. Remuzzi is also valued reviewer. Prof. Remuzzi is excellent scientist with great results in many fields: the understanding of the pathogenesis of bleeding tendency in patients with renal failure, evaluation of new therapeutic approaches for the treatment and prevention of uremic bleeding, observation of a plasmatic defect leading to a reduced vascular prostacyclin production in patients with thrombocytic thrombocytopenic purpura of haemolytic uraemic syndrome, and description of the therapeutic, understanding of the pathogenesis of pre-eclampsia and evaluation of prostaglandin metabolism in normal and complicated pregnancy, understanding of the pathogenesis of glomerulonephritis, clarifying the role of protein trafficking as a major determinant of renal disease progression in proteinuric renal diseases including the first description of genes that are upregulated in vitro and in vivo as a consequence of tubular protein overload; and many others. Prof. Remuzzi founded many research projects. From June 2013 until March 2015 he was President of the International Society of Nephrology (ISN), and he is the creator of the global ISN initiative called 0 by 25: Nobody should die of preventable and treatable Acute Kidney Injury (AKI) by 2025. Prof. Remuzzi has authored and co-authored more than 1247 scientific articles, reviews and monographs. In 2014 Prof. Remuzzi was recognized as Distinguished Fellow of ERA-EDTA (FERA).
Patient Choice of Renal Replacement Therapy… – which choice?!

EKHA is a common effort by stakeholders – among them ERA-EDTA – to propose solutions for the challenges of Chronic Kidney Disease in Europe through effective prevention and a more efficient care pathway intended to facilitate the provision of appropriate and affordable treatment to all Europeans equally, while promoting the highest quality of care. EKHA works on the principle that the issue of kidney health and disease must be considered at European level and that both the European Commission and European Parliament have vital roles to play in assisting national governments with these challenges. In the last years, EKHA has been very successful in arousing interest in kidney disease, its prevention and treatment among European politicians: A special MEP Group for Kidney Health acts as a debate forum to exchange and discuss information on kidney health and ensures the best possible realization into practice.

You initiated this MEP Group a few years ago. Why did you get interested in this topic? Before I got elected as an MEP to the European Parliament I was working as a member of the Parliament of Lower Austria, responsible for the health department. In this field I got confronted with the high costs of our health system and started causal research. I experienced that especially the increasing obesity in Europe, which is a main risk factor for chronic kidney disease (CKD), is an underestimated element of these high costs. Latest data show that nearly one person in every six aged 18 or over in the EU is obese and that non-communicable diseases such as cardiovascular disorders, stroke, type 2 diabetes and CKD are the cause of 86 percent of all deaths in the EU. We want to raise awareness for CKD as it receives far less attention than the other diseases correlated to obesity and as there is still no cure for it.

One major aim is to sensitize society and the political public sphere to the growing problem of chronic kidney disease. What measures have been taken by the group and which milestones have already been achieved? In order to raise awareness for CKD the MEP Group for Kidney Health constantly hosts and supports public events in this area. One of the milestones of our work is the successful adoption of motion for a resolution on industrial-produced trans-fatty acids (TFA) and is a significant step in preventing obesity and other diseases. We constantly work corresponding with our guiding principle: avoid, rather than treat.

At the 2017 European Kidney Forum in Brussels, EKHA Chairman Prof. Em. Raymond Vanholder presented the results of an online survey on the question “What is the reality of health inequalities in kidney care in Europe?”. The online survey had been answered by 662 patients and by 460 healthcare professionals of eight European countries (UK, France, Netherlands, Slovenia, Lithuania, Spain, Greece, Portugal) – and the results were surprising, if not shocking: Concerning the patient choice of treatment, there was a substantial heterogeneity amongst countries. Besides, there was no country where all options were proposed and explained to all patients. It seems that some sustainable options are not offered due to a lack of interest by the hospital/dialysis provider or due to the lack of specifically trained staff. Especially, the information on home dialysis was poor. Often, the patients do not know about sustainable options, which often results in a vicious circle (no patient information > no demand > no offering > therefore no patient information). “So, this is not only about treatment choices, but mainly about patient education”, commented Professor Vanholder. “We nephrologists have to make sure that the patients get all the information they need to make a proper treatment choice.”

Interview with MEP Karin Kadenbach

The MEP Group for Kidney Health is the informal group of Members of the European Parliament committed to improve the policy response to the growing burden of kidney disease in Europe. The MEP Group has been running since 2008, acting as a successful debate forum in topics such as sustainability of healthcare systems and health. In Brussels, we had the opportunity to talk to Ms Karin Kadenbach, chair of the MEP Group for Kidney Health about her personal commitment to kidney health and the work of her MEP group.

Mrs. Kadenbach, you are the Chairperson of the MEP Group for Kidney Health – what are the aims and objectives of this group? The main goal is to improve the policy response to the growing burden of kidney disease in Europe. This encompasses both prevention and access to best-practice care for all EU-citizens. Besides, the implementation and harmonization of organ donation and transplantation policies across the EU is another one of our goals. The MEP Group for Kidney Health acts as a debate forum to exchange and discuss information on kidney health and ensures the best possible realization into practice.

You initiated this MEP Group a few years ago. Why do you have kidney health at heart? How did you get interested in this topic? Before I got elected as an MEP to the European Parliament I was working as a member of the Parliament of Lower Austria, responsible for the health department. In this field I got confronted with the high costs of our health system and started causal research. I experienced that especially the increasing obesity in Europe, which is a main risk factor for chronic health issues.
Managing CKD, Diabetes & CVD: Is epigenetics a new way forward?

End-stage renal disease (ESRD) in children is a rare and challenging condition, and international collaboration is required to perform methodologically sound and clinically meaningful studies. Therefore, in 2007, the ESPN/ERA-EDTA Registry was launched. Currently, it is the world’s largest population-based registry for pediatric renal replacement therapy (RRT), including individual patient data for nearly 20,000 children from 38 European countries. The Registry has provided comprehensive data on health inequalities and practice variation in European pediatric RRT, and has provided information directly relevant to healthcare policy makers. The ESPN/ERA-EDTA Registry is a leading source of comprehensive data on pediatric RRT practices and outcomes in Europe and is celebrating its 10th anniversary this year.

At present, we are conducting a Registry study on recovery of renal function in European pediatric dialysis patients. Although, ESRD is defined as irreversible kidney failure requiring RRT to sustain life, a small number of chronic dialysis patients experience renal function recovery of their native kidneys. Recovery of renal function has rarely been reported, and then mainly in adult patients or in single-center studies. Single-center studies reported substantially higher recovery rates (as high as >5%) than large Registry studies (1%), which might be the result of a variable definition of renal function recovery and ESRD. Moreover, smaller studies usually include a higher number of patients starting dialysis with acute kidney injury leading to higher recovery rates.

The causes of recovery are not entirely clear. In adult dialysis patients the underlying renal disease seems to be one of the most predictive factors, but recovery can occur in almost any renal pathology. Higher recovery rates were observed in patients with autoimmune disorders with renal involvement, rapidly progressive glomerulonephritis, attherosclerotic and renal vascular disease, multiple myeloma, and cortical necrosis. In children with ESRD causes of renal failure highly deviate from adults.

From a clinical point of view, recovery of renal function may have implications for long-term planning of RRT, in particular when planning renal transplantation. Especially in children, rapid renal transplantation is regarded as the optimal mode of RRT, with better survival, physical and psychosocial outcomes. If renal function recovery is more likely in certain diseases, caution is required when considering an early transplantation strategy in these patients.

Therefore, we performed a study on renal function recovery among all European children included in the ESPN/ERA-EDTA Registry, who commenced dialysis between 1990 and 2014 at an age below 15 years (n=6597). Our data, in the largest cohort of pediatric chronic dialysis patients studied to date, show the possibility of recovery of renal function, even after several months on dialysis. Furthermore, we found that patient age and cause of renal failure were the main determinants of renal function recovery. These data will be presented during the ERA-EDTA Registry Symposium on Sunday June 4th. For more information on the ESPN/ERA-EDTA Registry please visit our website: www.espn-reg.org

**ERA-EDTA Registry**

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**Managing CKD, Diabetes & CVD: Is epigenetics a new way forward?**

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Modification of the ‘long gap’ phenomenon by HD treatment time

Observational studies have repeatedly shown increases of 20–40% for mortality and 40–70% for hospitalization after the two-day break (Monday and Tuesday) in patients dialyzing three times a week.

Postulated mechanisms include the effects of fluid overload and the need to rapidly remove fluid during the dialysis session. Peak concentrations of toxins including potassium increase the risk of arrhythmias and sudden death, manifesting in higher rates of sudden or out-of-hospital death. Longer dialysis session length has beneficial associations with all these mechanisms, but its impact on events after the two-day break has not been explored. Importantly, longer treatment times can be delivered in the three-times-a-week pattern, and have been shown to be more acceptable than additional dialysis sessions. On the 2nd June at 8.00 am we will provisional-lly report our study on data from 19,585 European three-times-a-week hemodialysis (HD) patients collected through the Dialysis Outcomes and Practice Patterns Study (DOPPS), as part of the EURODOPPS program. Led by Dr James Fotheringham, who is funded by the UK’s Membranous nephropathy phenomenon by HD treatment time.

To understand if longer treatment times reduce these excess events after the two-day break, we grouped patients into those receiving treatment times of < 200 minutes, 200–225, 226–250 and > 250 minutes three times a week, and compared the mortality and hospitalization rates after the two-day break compared to the rest of the week. We adjusted for patient-level and facility-level characteristics using a Cox Regression model. Despite an overall hazard ratio for mortality of 0.80 (95% CI 0.77–0.84) and hospitalization of 0.98 (95% CI 0.94–0.99) for each 30 minutes longer treatment time, we could still see harm specifically after the two-day break (Figure 2). The hazard ratio for mortality after the two-day break compared to the rest of the week was 1.66, 1.54 and 1.36 for 200–225, 226–250 and > 250 minutes (all p < 0.005), with those dialyzing < 200 minutes having very high overall mortality but no two-day break effect. Out-of-hospital mortality showed a similar pattern. The hazard ratio for hospitalization after the two-day break compared to the rest of the week was between 2.03 and 2.14 for all four groups, and between 2.50 and 3.62 for hospitalization for heart failure and fluid overload (all p < 0.001).

Mortality and hospitalization rates after the two-day break
diagram

All-cause mortality rate was 17 per 100 patient years the first day after the two-day break compared to 13 across the rest of the week (adjusted hazard ratio (HR) 1.38, 95% CI 1.27–1.50). All-cause hospitalization was 1.5 per patient year after the two-day break compared to 0.7 for the rest of the week (HR 2.1, 95% CI 2.02–2.17). Larger increases were seen in out-of-hospital death and hospitalization for fluid overload. Figure 1 shows these rates across the dialysis week, with HD1, HD2 and HD3 representing the days patients receive HD.

Recognizing that there would be some bias introduced by the use of longer treatment times in patients who were more comorbid, we also performed an instrumental variable analysis which utilizes different practice patterns across dialysis facilities as a form of randomization. This was effective in reducing bias, but still showed that there was no reduction in the hazard ratio for two-day break events with longer treatment times. We look forward to presenting our broader findings during our talk on the 2nd June.

We hoped that the overlap between the proposed mechanisms for the harm caused by the two-day break and the observed benefits for longer treatment times would mean a reduction in the risk after the two-day break in patients dialyzing for longer times three a week. We could find no evidence of this for the endpoints of all-cause mortality and hospitalization, out of hospital death, hospitalization for heart failure and fluid overload. Although a better understanding of how the two-day break causes harm might be appealing, understanding specifically who is at risk, when, and the role of additional HD sessions in this setting may improve outcomes sooner.

Membranous nephropathy – what is new in 2017?

Membranous nephropathy (MN) is a major cause of nephrotic syndrome in people over 50 years of age. It is characterized by the presence of immune deposits on the outer aspect of the basement membrane. These deposits consist of Ig specific for antigens that have long eluded identification and of the membrane attack complex of complement (MAC). Circulating antibodies bind to their target antigen on the podocyte, induce the formation of immune deposits that activate complement to the formation of MAC, which in turn induces cell injury and proteinuria.

MN has been continuously evolving since the identification of neutral endopeptidase (NEP) and phospholipase A2 receptor (PLA2R), as the target antigens in neonatal and adult MN. Although one cannot exclude a substantial level of cross-reaction to other antigens in neonatal and adult MN. Although one cannot exclude a substantial level of cross-reaction to other antigens in neonatal and adult MN.

A new antigen (THSD7A) and more on PLA2R-associated second- ary membranous nephropathy

The new podocyte antigen thrombospondin Type-1 Domain-Containing 7A (THSD7A), identified by two groups in Boston and Hamburg, bears structural similarities with PLA2R and is associated with less than 5% of PLA2R-negative MN. Antibodies against this antigen can be detected by a new immunofluorescence test (Euroimmun AG) comparable to that used for PLA2R. At variance with PLA2R, THSD7A is expressed in mouse podocytes, which allowed transfer of the disease by infusion of antibodies purified from patients.

One important characteristic of THSD7A-associated MN is its potential association with cancer. The THSD7A antigen has indeed been identified in tumor cells (derived from gallbladder or uterus) and in metastatic lymph nodes both in tumor cells and dendritic cells, thus providing a link between the tumor and the renal disease. It might well be that a subset of paraneoplastic MN is caused by immunization against THSD7A, but further epidemiological studies are needed to confirm the preferred association with THSD7A.

Although it is generally considered that PLA2R detection in immune deposits is specific for primary MN, we have identified two situations where this occurs in secondary MN: active sarcoidosis and hepatitis B with viral replication in Africans (a similar observation was made about epitope spreading in about 60% of Chinese patients with MN). Although one cannot exclude a coincidence between the two diseases, we suggest that the immunological alterations associated with sarcoidosis and hepatitis B favor the development of autoimmune PLA2R-related MN. Therefore, patients with PLA2R antigen deposits in glomeruli should not systematically be considered as having primary MN.

More on complement pathways

Although complement activation is the major mediator of proteinuria, pathways of complement activation remain elusive, one main reason is that...
Is there a role for iron beyond erythropoiesis in patients with chronic kidney disease?

Chair: Professor Danilo Fliser

Sunday 4 June 2017
13:30–15:00

Hall 10.B, IFEMA Feria de Madrid
(North Congress Centre)

Objectives

- Discuss benefits of treating non-haematological effects of iron in nephrology
- Review clinical evidence from cardiology studies and interpret them from a nephrologist’s perspective

Programme

13:30 Lunchboxes will be provided

13:45 Chair’s welcome and introduction
Danilo Fliser (Saarland University Medical Centre, Homburg, Germany)

13:55 Interactive panel discussion
Open panel discussion based on expert experience and recommendations for treating iron deficiency
Danilo Fliser
Iain Macdougall (King’s College Hospital, London, UK)
Carlo Gaillard (University of Utrecht Medical Centre, Utrecht, The Netherlands)
Austin Stack (Health Research Institute, Limerick, Ireland)
Josep Comin-Colet (Bellvitge University Hospital, Barcelona, Spain)
Darlington (Obi) Okonko (King’s College Hospital, London, UK)

Meeting close

www.era-edta2017.org
IgA-nephropathy: what is new in 2017?

IgA4, which does not or only weakly activates complement, is the prevailing subclass deposited in glomeruli. In primary MN, the absence of C1q practically rules out the classical pathway. In this context, the frequent presence of C4d favors activation of the mannose-binding lectin (MBL) pathway. On the other hand, the presence of factor B and properdin points to the alternative pathway. Thus, it is generally considered that both the MBL and AP are activated. We had the opportunity to investigate a young man with numerous ENT infections in childhood who developed full-blown MN with nephritic syndrome. We found that this patient was antigenically, functionally, and genetically deficient in MBL. In IgAN, we confirmed this finding in our recent randomized controlled trial (GERMITION), which first showed the efficacy of rituximab against anti-proteinuric therapy alone. Patients with reactivity with the immunodominant epitope (Cy8R) only, had a higher chance of spontaneous remission. By multivariate analysis, epitope spreading at baseline was an independent predictor of clinical remission at 6 months and last follow-up, irrespective of PLASR-rider at baseline, age, gender, and treatment group.

At variance with antibodies, the role of T-cells in MN has been neglected. We found a decreased frequency of Treg among CD4 T-cells compared to age-matched healthy donors. Unexpectedly, Treg % among CD4 cells and Treg absolute numbers were increased during treatment with rituximab in our GERMITION trial. Responder patients were characterized by a lower Treg % at baseline, and by a significant increase of Treg % observed at day 8, 3 months and 6 months, whereas Treg remained unchanged in non-responder patients and in those treated with antiproteinuric therapy alone. These results, which should be confirmed in larger series and validation cohorts, suggest that Treg cell dynamics might be early predictors of response to rituximab.

References

Session 3.3
Gloomerulonephritis: What is new in 2017?
Sunday, 08.00–09.30, Hall N103–104

References

Session 3.3
Gloomerulonephritis: What is new in 2017?
Sunday, 08.00–09.30, Hall N103–104
SGLT2 inhibition and renal pathophysiology

The kidney utilizes glucose as a substrate, plays an important role in gluconeogenesis, and reabsorbs the glucose filtered in the glomerulus back to the circulation at the level of the proximal tubule. Glucose tubular reabsorption is mediated by an energy-dependent sodium-coupled glucose transporter called SGLT2. In normal physiology, around 180 grams of glucose are filtered and completely re-absorbed by the kidneys’ proximal tubules every day. In individuals without diabetes, if plasma glucose concentration rises over around 180–200 mg/dl the capacity of SGLT2 transporters is exceeded, and excess filtered glucose appears in the urine, resulting in glycosuria. In patients with diabetes, the renal tubular reabsorption of glucose is increased secondary to an upregulation of the SGLT2 transporters. The increased expression of SGLT2 transporters results in increased glucose reabsorption; however uncontrolled hyperglycaemia results in plasma glucose that is still above the ‘higher’ renal glucose threshold seen in patients with diabetes, leading to glycosuria.

Recently SGLT2 dysregulation in diabetes has become a target for treatment. In studies, blocking the action of SGLT2 in patients with type-2 diabetes has resulted in an improvement in glycemic control paralleled by weight loss and by a modest, but clinically significant, fall in systolic and diastolic blood pressure. The SGLT2 inhibitors’ mode of action is insulin independent and rarely results in hypoglycaemia unless the SGLT2 inhibitor is utilized in conjunction with insulin or beta cell secretagogues (e.g. sulphonylurea).

Recent clinical trials have demonstrated an important cardiovascular and renoprotective effect of the SGLT2 inhibitor empagliflozin and recent parallel work suggests that this might be a class effect of the SGLT2 inhibitors. The precise mechanism(s) by which SGLT2 inhibitors exert their cardiorenal protective effects are currently unknown. Different theories/possibilities have been postulated and research is ongoing to better define the cardiorenal protective effects of SGLT2 inhibitors. In line with the rapid (~6–12 months) observed cardiorenal vascular protective effects of SGLT2 inhibitors, two major theories have been postulated:

(1) Intrarenal theory: this theory postulates that the SGLT2-mediated renoprotective effect is secondary to activation of tubuloglomerular feedback with secondary reduction in glomerular capillary pressure, and a parallel inhibition of enhanced tubuli sodium-coupled glucose transport that would result in reduction of tubulointerstitial injury. Further, the use of SGLT2 inhibitors in combination with inhibitors of the renin-angiotensin-aldosterone system could also result in upregulation of angiotensin 1–7 in known to retain a vasodilatory, anti-inflammatory and anti-oxidative stress protective effects.

(2) Systemic theory: the systemic theory suggests that plasma volume contraction (driven by SGLT2-mediated glycosuria and possibly natriuresis) and blood pressure reduction observed with SGLT2 therapy could be at the basis of the cardiorenal protective mechanisms of this new class of drugs.

In conclusion, SGLT2 inhibition is an important novel tool that can be utilized for the treatment of hyperglycaemia in patients with type 2 diabetes. Studies are ongoing to understand the role of these compounds in reducing the burden of chronic diabetic cardiovascular-renal complications.
Consider SGLT2 inhibitors for high-risk type 2 diabetes patients

There is increasing evidence that sodium glucose cotransporter 2 (SGLT2) inhibitors have renoprotective effects, as demonstrated by the renal analyses from clinical trials including EMPA-REG OUTCOME®. The potential mechanisms responsible for the improved renal outcomes observed with SGLT2 inhibition are likely to be multifactorial; direct renovascular and hemodynamic effects are postulated to have a key role.

There is increasing evidence that these drugs have renoprotective effects

SGLT2 inhibition reduces proximal tubular sodium reabsorption, and thus increases sodium delivery to the macula densa, which activates tubuloglomerular feedback and afferent arteriolar vasomodulation, resulting in decreased renal blood flow and decreased glomerular hyperfiltration. Empagliflozin has been investigated first in a cardiovascular outcome study where renal events were the prespecified secondary outcomes. However, the described mechanisms are also seen with other SGLT2 Inhibitors and outcome data are awaited.

The EMPA-REG Outcome study population included patients with type 2 diabetes (T2D), established cardiovascular disease, and an estimated glomerular filtration rate (eGFR) ≥30 mL/min/1.73 m². Patients were randomized (n=7,020) to receive either empagliflozin (10 mg or 25 mg) or placebo once daily, in addition to standard care. The prespecified renal outcome was called incident or worsening nephropathy and was a composite including several subcomponents (Figure). Empagliflozin treatment was associated with a statistically significant 39% reduction in relative risk of incident or worsening nephropathy versus placebo. Statistically significant relative risk reductions were also observed for progression to macroalbuminuria (a component of incident or worsening nephropathy), doubling of serum creatinine levels, and the initiation of renal replacement therapy (Figure). Events consistent with acute renal failure (including acute kidney injury) and hyperkalemia occurred less frequently in the empagliflozin group than in the placebo group. Mean eGFR decreased over the first 4 weeks and then stabilized in the empagliflozin group compared with placebo, which is suggestive of decreased intraglomerular pressure. Among patients in the empagliflozin group, the adjusted mean difference from placebo in the change from baseline in eGFR was 4.7 mL/min/1.73 m² (p<0.001).

The excretion of glucose through SGLT2 inhibition (approximately 80 g/day), lowers HbA1c and causes osmotic diuresis and natriuresis. SGLT2 inhibitors also decrease blood pressure, decrease body weight, decrease albumin excretion by about 30%, are uricosuric, and do not raise sympathetic nerve activity. All these effects may translate into the prominent reductions in cardiovascular mortality and all-cause mortality (Figure). It is noteworthy that the reductions in hospitalization due to heart failure occur rapidly and are attributed to the reduction in extracellular volume following osmotic diuresis.

The renal benefits of SGLT2 inhibitors, as well as the cardiovascular benefits of empagliflozin, should be considered by all physicians when selecting glucose-lowering medication for the management of patients with T2D and high cardiovascular risk. The renal findings from clinical trials of empagliflozin, dapagliflozin and canagliflozin can be more definitively be assessed in mid-June 2017, when results from the CANVAS and CANVAS-R (CANagliflozin cardioVascular Assessment Study-Renal endpoints) will be presented at the American Diabetes Association conference.

Session 8.3
SGLT-2 inhibitors in diabetic kidney disease
Sunday, 08.00–09.30, Hall 10

PLENARY LECTURES

Whole-body and whole-organ clearing and imaging
Hiroki Ueda
Sunday, 10.45–11.30, Hall 10 Plenary

Re-Creating Life
Steve Benner
Monday, 10.45–11.30, Hall 10 Plenary

Comparative effectiveness research in nephrology: using electronic health records to emulate randomized trials
Miguel Hernandez
Tuesday, 09.45–10.30, Hall 10 Plenary
SGLT2 inhibition: physiology and pathophysiology

The kidney plays an important role in the control of plasma glucose concentration. It produces glucose by gluconeogenesis and reabsorbs the glucose filtered by the glomerulus. Renal glucose reabsorption takes place exclusively in the proximal tubule through glucose carriers. The sodium glucose transporter type 2 (SGLT2) encoded by SLC5A2 gene is expressed at the apical membrane of the renal proximal tubular cells. It uses the sodium gradient to remove most of glucose from urine. Then glucose returns to the blood through the facilitative glucose transporter 2 (GLUT2) that is expressed at the basolateral side of the cells. As glucose urine concentration decreases along the proximal tubule SGLT2 expression is replaced by SGLT1, a transporter with higher affinity for glucose but lower transport capacity, and GLUT2 by GLUT1.

In diabetes the kidney becomes resistant to insulin action, which increases the renal expression of the gluconeogenesis enzymes and of SGLT2 and GLUT2. These modifications are subsequent to the elevation of transcription factor HNF1α expression. Consequently, while plasma glucose concentration rises, the ability of the kidney to produce glucose and to reabsorb glucose from urine increases. Hence the kidney exacerbates the rise in plasma glucose concentration in diabetes.

Animal models have suggested that inhibiting renal SGLT2 expression or activity in the presence or in the absence of diabetes significantly increases urine glucose excretion. In diabetic animals, inhibition of SGLT2 activity improves plasma glucose concentration. Loss of function mutations in human SGLT2 leads to normoglycemic glycosuria. The majority of patients with a SGLT2 mutation do not seem to develop any clinical problem over time. In animals and in humans with diabetes, SGLT2 inhibitors improve plasma glucose concentration and have been approved by health agencies in Europe and in North America for the treatment of diabetes.

Beyond their effect on glucose homeostasis, SGLT2 inhibitors reduce the renal hyperfiltration observed in the initial stages of diabetes in various animal models and in humans. This effect could be the consequence of the stimulation of the tubuloglomerular feedback, the decrease in glucose uptake in the proximal tubule induces a decrease in Na and Cl reabsorption leading to the constriction of the afferent arteriole. Furthermore SGLT2 expression has been detected in mesangial cells and could directly regulate their contractility.

In human with diabetes, and in some animal models, SGLT2 inhibitor treatment has been associated with a slower deterioration of renal function and a reduction in albuminuria. These beneficial effects could be the consequence of the reduction of the intraglomerular pressure. SGLT2 inhibition has also been associated with a decrease in systolic blood pressure that could be attributed to the augmentation of natriuresis. A diminution of the risk of cardiovascular outcomes and mortality has been reported in a large clinical trial. However it is uncertain if these protective effects were specific of the inhibitor studied or are a more general property. Indeed, studies with other inhibitors did not observe this beneficial effect.

The use of SGLT2 inhibitors has raised several concerns. Calcium reabsorption in the renal proximal tubule is coupled to water reabsorption that is driven by glucose uptake. SGLT2 inhibitors increase urinary calcium loss that can result in deterioration in bone microarchitecture and bone strength in animals. An increase in bone fracture rate has been reported among older patients treated with an SGLT2 inhibitor in a clinical trial, suggesting that calcium intake should be carefully monitored.

Type 2 diabetes is characterized by insulin resistance, a defect of insulin secretion and also inappropriate over-production of glucagon. Recently SGLT2 expression has been identified in glucagon-secreting alpha cells. It is controlled by HNF4α. Inhibition of SGLT2 activity in these cells triggers glucagon secretion through KATP channel activation. In diabetic patients treated with an SGLT2 inhibitor, glucagon secretion and endogenous glucose production are increased. Similar results were observed in healthy mice suggesting that SGLT2 plays a role in the control of glucagon secretion in physiological conditions. By contrast with the kidney, SGLT2 expression is decreased in pancreatic alpha cells from diabetic patients, contributing to the overproduction of glucose and the increase in hepatic gluconeogenesis.

Treatment with SGLT2 inhibitors not only improves plasma glycemic control but also contributes to a significant reduction in body weight. This effect is observed in diabetic patients and also in obese adults without diabetes. The loss of weight is attributed to a reduction of adipose tissue without change of lean tissue.

SGLT2 inhibitors in diabetic kidney disease

Sunday, 08.00 – 09.30, Hall 10
**Meeting the emerging threat of Clostridium difficile**

Clostridium difficile is a Gram-positive, anaerobic spore-forming bacillus. It is currently one of the most frequent pathogens causing antibiotic-associated diarrhea and the main cause of nosocomial diarrhea. The main factor determining the pathogenicity of C. difficile is the production of bacterial toxins A and B that cause damage to the mucosa of the gut, leading to a disease associated with C. difficile in approximately 25% of patients. The main factor determining the risk factors are: older age, hospitalization, drugs and probiotics and especially the Lactobacillus plantarum 299v strain can be considered.

**Clostridium difficile infection is now frequently observed in patients in the nephrology**

CDI was first described in CKD patients in 1985, and there has been a recent increase in prevalence among patients hospitalized in the nephrology ward. A meta-analysis of 20 studies showed a significantly increased risk of CDI and CDI recurrence in CKD patients (1.9-fold and 2.6-fold increased risks, respectively). Patients with CKD stages 4 and 5 or CKD patients treated with chronic hemodialysis are characterized by increased risk of CDI (OR=2.90 and OR=3.34, respectively). Furthermore, CDI is associated with increased mortality in patients with advanced CKD.

The increased risk of CDI in CKD patients might be caused by frequent antibiotic therapy, frequent hospitalizations, the older age and immunosuppressive therapy. Since CKD patients are characterized by high CDI risk, prevention in these patients becomes an issue of great importance. Among CDI preventive measures, use of probiotics and especially the Lactobacillus plantarum 299v strain can be considered. LP299v is a Gram-positive, lactococcal acid bacterium that naturally occurs on the surface of human intestinal mucosa. This strain has specific properties in the colonization of human intestine due to mannose-dependent adhesion to the epithelium of human intestines. Mannose-dependent adhesion of LP299v leads to inhibition of bacterial translocation from the intestinal lumens into the blood vessels. In the general population it has been shown that administration of a strain LP299v reduces the severity of gastrointestinal adverse effects during antibiotic therapy.

A retrospective study was performed in the Department of Nephrology, Transplantation and Internal Medicine, Medical University of Silesia, Katowice, Poland, with the aim of assessing the efficacy of the LP299v strain in the prevention of CDI. A two-year observation period was divided into two twelve-month intervals: before and during use of LP299v as routine CDI prophylaxis in high-risk patients (i.e. patients receiving antibiotic therapy or immunosuppressive treatment).

**Calcium transport: insights from mathematical modeling**

Keeping the extracellular concentration of calcium within tight bounds is essential to prevent unwanted biominarization in tissues other than bone and teeth, since calcium has a high propensity to constitute microrystals. The homeostasis of calcium is maintained by continuously adjusting its intestinal absorption, bone accretion, resorption, renal reabsorption, and urinary excretion. These fluxes are regulated principally by parathyroid hormone (PTH), calcitriol (i.e. the active form of vitamin D3), and calcium itself, via positive and negative feedback loops (Figure 1). The secretion of PTH into plasma is in turn modulated by the calcium-sensing receptor (CaSR) at the surface of parathyroid cells.

The kidneys excrete a small fraction (~1–2%) of the filtered load of Ca2+. The proximal tubule reabsorbs about two-thirds of the Ca2+ load, and the thick ascending limb (TAL) 20–25%, in these nephron segments, Ca2+-transport is paracellular and driven by Na+ reabsorption. The renal excretion of Ca2+ is fine-tuned in the late distal convoluted tubule and the connecting tubule, where Ca2+-reabsorption is transcellular and mediated by transient receptor potential channels vanillain subfamily 5 (TRPV5) on the apical side, and by Na+/Ca2+ exchangers (NCX1) and plasma membrane Ca2+ pumps on the basolateral surface. Recent studies have shown that transcellular and paracellular Ca2+-transport is mediated by PTH, calcitriol, and/or renal CaSR. Preserving a low Ca2+ concentration ([Ca2+]i) in the urinary filtrate is essential to prevent the formation of calcium stones.

Recent work on renal Ca2+ handling has focused on the molecular transporters and sensors of Ca2+. To obtain an integrated and quantitative understanding of the impact of regulatory mechanisms on renal Ca2+ handling and urinary excretion, we have built over the last few years several mathematical models of calcium transport at different scales. We have sought in particular to elucidate the contribution of the Ca2+-sensing receptor in the TAL, which has been shown to regulate the paracellular permeability of the TAL to Ca2+ (Loupy et al., 2012). This ‘direct’ effect is predicted to significantly modulate urinary Ca2+ excretion under both hypercalcemic and hypocalcemic conditions. We have assessed ‘indirect’ effects as well, that is, the extent to which the impact of CaSR on Ca2+-reabsorption in the TAL may be further amplified if CaSR also modulates transcellular NaCl transport in that segment. Two other Ca2+-sensing mechanisms are thought to help reduce Ca2+-precipitation in the collecting duct; in vitro studies have found that luminal [Ca2+]i in the collecting duct upregulates the activity of H+-ATPase pumps and reduces the water permeability imparted by AQP2 water channels. Our model also sheds light on the contribution of these two mechanisms to the regulation of luminal [Ca2+]i and urinary pH.

A larger-scale model describes the renal handling of Ca2+ in both the tubular and vascular systems, without explicitly representing the proteins that mediate apical and basolateral transport. It predicts that there is a significant axial Ca2+ concentration gradient along the cortico-medullary axis, which stems from the passive diffusion of Ca2+ from the loops of Henle and vasa recta into the interstitium. The interstitial Ca2+ concentration gradient is markedly dependent on the permeability of descending vasa recta to Ca2+ according to our model, and experimental measurements of the latter would be very valuable.

We also developed a model of calcium homeostasis at the organism level, which represents Ca intestinal uptake, bone resorption, accretion, and urinary excretion, and the hormonal regulation of these fluxes. It also accounts for the presence of a rapidly exchangeable Ca2+ pool in bone. The model was employed to elucidate the intricate feedback mechanisms in vitamin D3 deficiency, and in primary hyper- and hypoparathyroidism. In particular, our results indicate that the counterbalancing effects of PTH and CaSR on Ca2+-reabsorption in the TAL may underlie, at least partly, the high variability of hypercalcemia that is observed in patients with primary hyperparathyroidism. We aim to expand these Ca2+-transport models to gain a better understanding of the factors that lead to dysregulation of calcium and phosphate homeostasis in chronic kidney disease.
Management of CKD-MBD: time for new concepts?

Sunday 4 June 2017
18.45–19.45
Hall 10.B, IFEMA Feria de Madrid

Chair: Professor Markus Ketteler, Germany

Programme

18.45 Chair’s introduction: how new evidence is guiding the guidelines
Markus Ketteler, Germany

18.55 Management of MBD on dialysis: how can we improve the control of hyperphosphatemia?
Jürgen Floege, Germany

19.15 Treatment of MBD before reaching ESRD: what is the role of 25(OH)D₃?
John Cunningham, UK

19.35 Q&A and meeting close
Markus Ketteler, Germany

Light refreshments will be provided prior to the symposium
We consume daily between 1000–2000 mg of inorganic phosphate, far exceeding our daily phosphate requirements. Since most of this phosphate is readily absorbable in the small intestine, and because intestinal phosphate absorption is only partly regulated and adapted to phosphate intake, the kidneys must act as the gatekeeper of systemic phosphate homeostasis.

Renal control of phosphate involves glomerular filtration and subsequent reabsorption of phosphate by the proximal tubule. Depending on the filtered load (glomerular filtration rate x plasma phosphate levels) and the rate of proximal tubule reabsorption, the kidney will excrete more or less phosphate.

Tubular phosphate reabsorption is mostly initiated and mediated by a set of phosphate transporters located in the luminal brush border membrane of the proximal tubule: the sodium-dependent phosphate transporters NaPiIIa (SLC34A1), NaPiIIc (SLC34A3), and PiT2 (SLC20A2). Genetic evidence from patients with inherited forms of renal phosphate wasting demonstrates the importance of these transporters in renal phosphate handling. Patients with autosomal recessive mutations in SLC34A1 (NaPiIIa) often develop severe hypercalcemia subsequent to renal loss of phosphate with compensatory stimulation of vitamin D3 and excessive intestinal calcium absorption, causing hypercalciuria, nephrocalcinosis, and progressive loss of renal function. Similarly, mutations in SLC34A3 (NaPiIIc) cause a similar disease but may be combined with rickets. In the case of SLC20A2 (PiT2) mutations, patients develop basal ganglia calcifications, patients with XPR1 mutations develop basal ganglia calcification, but no problems with systemic phosphate balance have been reported, suggesting that PiT2 contributes only little to overall renal capacity to reabsorb phosphate.

The pathway releasing phosphate from proximal tubule cells into blood (thereby completing the transcellular absorption of phosphate) is not well understood. Recently, the xerotopic and polytrophic ronotronic receptor 1 (XPR1) has been implicated in either controlling basolateral phosphate release or mediating transport of phosphate as part of a transport system. However, patients with XPR1 mutations develop basal ganglia calcification, but no alterations in phosphate balance have been reported. In contrast, mice with deletion of Xpr1 develop a severe Fanconi-syndrome and die early. Thus, the role of XPR1 in renal handling will require further clarification.

The abundance and activity of renal phosphate transporters and hence phosphate reabsorption are actively and tightly regulated. Low phosphate intake results in a stimulation of phosphate reabsorption, whereas high phosphate intake (in most industrialized countries the default situation) reduces renal phosphate reabsorption, hence enhancing phosphaturia. A variety of endocrine and metabolic factors including parathyroid hormone (PTH), active vitamin D3, fibroblast growth factor 23 (FGF23), together with cAMP, dopamine, glucocorticoids, growth hormone, insulin-like growth factor, acid-base status, and electrolytes impact on renal phosphate handling.

PTH and FGF23 both play a particularly critical role in stimulating renal phosphate excretion by downregulating the expression of phosphate transporters. In both humans and rodents, intake of a phosphate-rich diet triggers a rapid renal response to excrete phosphate. It had been previously suggested that this may be initiated by a gut-derived signal, but recent studies refuted this idea as no evidence for such signals could be detected. In contrast, a rapid rise in PTH occurs and, at least in rats, PTH is critical for the early phosphate response and for normalization of phosphate balance. PTH will induce the internalization and degradation of renal phosphate transporters.

FGF23 rises only with a delay of several hours after the intake of phosphate (or elevation of plasma phosphate) and the exact mechanisms how FGF23 induces phosphaturia have not been clarified. Currently, at least two alternative models of direct signaling in the proximal tubule versus an indirect signal emanating from the distal convoluted tubule are discussed. It is also unclear how changes in phosphate balance translate into the regulation of FGF23 levels; whether phosphate alone is sufficient to induce FGF23 release from bone has been debated.

The latter question is of importance, as it may also help to answer the question how and why FGF23 rises early in the course of chronic kidney disease (CKD). Associations between inflammatory cytokines and FGF23 in patients with CKD and in vitro data suggesting that several proinflammatory cytokines can stimulate osteocyte production of FGF23 link inflammation with FGF23 may provide an additional explanation for high FGF23 levels in CKD. In early CKD, elevated FGF23 may be on the one hand beneficial by stimulating renal excretion of phosphate, but on the other hand it exerts detrimental effects by suppressing 1,25-(OH)2 vitamin D3 synthesis that contribute to the development of secondary hyperparathyroidism.

Undoubtedly, the kidney is the central organ in controlling and maintaining phosphate homeostasis, causing the well-known problems of mineral and bone disorders in patients with CKD. However, many open questions ranging from mechanisms of tubular phosphate transport to the endocrine control of phosphate balance and its dysregulation in CKD remain to be clarified.
What is the evidence for BP control in PD?

**James Heaf**

Academic, Denmark

In the absence of large clinical studies addressing the question of optimal treatment of hypertension in peritoneal dialysis (PD), the clinician has to refer to comparable groups: patients with normal renal function (N), chronic kidney disease (CKD) and hemodialysis patients (HD). The International Society for Peritoneal Dialysis (ISPD) recommendation of a blood pressure (BP) of <145/90, in line with the general population, is therefore rational. The British Renal Association is more conservative: in the absence of convincing epidemiological or therapeutic evidence for active treatment, a systolic BP > 160 should be avoided. The KDQI guidelines do not have any specific recommendation.

The question of the method of BP assessment is important. Ambulatory BP measurements, using either automated 24-hour or patient measurements, are necessary to exclude white-coat hypertension and diagnose masked hypertension. Since home or 24-hour BP measurements are used instead of the usual before- and after-HD measurements, a more normal correlation is seen; reverse epidemiology is, however, also seen in PD. Hypertension is probably also a marker of progressive cardiac failure. Dialysis patients are characterized by arterial calcification, arterial stiffness and a high pulse pressure. Since coronary perfusion occurs mainly during diastole, a low diastolic pressure may theoretically cause myocardial ischemia. Based on epidemiology, a cautious approach would be to avoid reducing the blood pressure below 120/70 mmHg.

Non-dipper status is associated with increased cardiovascular disease (CVD) and death, both in N, HD and PD, and moving at least one antihypertensive drug to the evening reduces CVD in N. Non-dipper status is very common in dialysis; thus, a similar practice in PD is rational. Sleep apnea is also common in dialysis, and is associated with resistant hypertension, non-dipper status and mortality in HD. However, evidence of a beneficial effect of continuous positive airway pressure therapy (CPAP) treatment is lacking.

The prevalence of hypertension in PD is high and is mainly related to overhydration. The primary treatment of hypertension is therefore fluid control, and furosemide and zoledronate to maintain a diuresis > 2 l/day is the primary pharmacologic therapy. Spironolactone in addition to its diuretic properties reduces cardiac fibrosis in N, it prevents peritoneal fibrosis in PD-treated rats; it is antihypertensive in N, HD and PD. Carotid intima media thickness (CIMT) is reduced in HD and left-ventricular hypertrophy (LVH) is present in HD and PD, even in oliguric patients.

The DOHAS study demonstrated a reduction in death and cerebrovascular and cardiovascular events in HD, while a recently published study of dialysis patients, 39% of whom were on PD, showed reductions in cardiovascular and total mortality, LVH, and BP medication, and improvements in flow-mediated vasodilation and ejection fraction. Spironolactone is thus to be generally recommended for both hypertensive and non-hypertensive dialysis patients. The primary contraindication is hyperkalemia, but this is rarely a problem in PD.

The evidence for specific antihypertensive treatment is more controversial. Surrogate measures of a protective effect on mortality – e.g., LVH and CIMT – must often be accepted. Most studies are performed on HD patients. These treatments are characterized by a highly variable BP and cardiovascular stress during dialysis; their findings may not be directly applicable to PD. With these caveats, randomized controlled trials suggest a beneficial effect of pharmacologic treatment.

Residual renal function (RRF) is better preserved in PD than HD, and is a major, probably causal, marker of survival. Progressive peritoneal fibrosis is a major cause of technique failure, and therapies that prevent this are to be preferred. Renin-angiotensin blockade (RAS-B) is therefore an attractive treatment in PD. Just as in CKD generally, RAS-B reduces the rate of RRF loss. Theoretical considerations suggest that it protects against peritoneal fibrosis, and animal studies confirm this. It is associated with better preservation of the peritoneum in PD. There is however one major counterfactual. The HDFAL study randomized HD patients to either β-blocker (atenolol) or ACE-I (lisinopril) treatment for 12 months. Despite a greater reduction in weight, BP was higher in the ACE-I group, which required more supplementary antihypertensive treatment. Serious CV events, particularly heart failure, were more common in this group.

One major cause of hypertension in CKD is increased sympathetic activity, which is also associated with mortality in HD. These findings suggest that this is also a major factor in CVD, and that β-blocker treatment should be an integral element in antihypertensive treatment of HD patients. Whether these findings are relevant for PD patients is unknown. The question is academic for many PD patients, who will often require several different drugs to control their blood pressure.
Hyperkalemia in dialysis: what is on the horizon?

Matthew R. Weir
Seattle, United States of America

It is well known that hyperkalemia is prevalent among people on dialysis. It leads to numerous emergency-room visits and increased healthcare costs. This is no different from what is seen in clinical practice in people with advanced heart or kidney disease. Moreover, it is well known that the adjusted mortality by serum potassium is markedly greater with increasing age and associated medical comorbidity.

Serum potassium concentration is very carefully regulated by a variety of different hormonal and other systems, including the renin-angiotensin system (RAS), the sympathetic nervous system, as well as the release of insulin. All of these will either facilitate cellular uptake of potassium or increase gastrointestinal (GI) or renal excretion. The GI tract takes on greater responsibility for excreting potassium as a patient’s kidney function declines; whereas normally the colon may be responsible for about 10%, this may increase up to 30% in people with end-stage renal disease.

There are also issues related to hyperkalemia due to impaired extrarenal buffering, insulin deficiency, beta blockers, autonomic insufficiency and cardiac glycodies such as digoxin. They interfere with the normal shift of potassium inside cells and sodium and/or hydronium ions outside the cell.

Many issues remain with regard to the treatment strategy for hyperkalemia in dialysis patients. One of the most important issues is the chronicity versus the acuity of change in serum potassium. Chronic changes are very well tolerated; however, elevated levels of serum potassium also pose a risk for the patient, in that perturbations that can lead to higher levels of serum potassium from a much higher baseline may be associated with arrhythmias.

Hemodialysis (HD) itself can remove 25 – 50 mEq of potassium per hour depending on the gradient, blood flow, type of dialysis and of course duration of the treatment. However, there is also a post-dialysis rebound that occurs within a few hours of dialysis cessation. There is concern about the size of gradient that is established between dialysate potassium level, which is often 2 or 3 mEq/L, and the patient’s ambient serum level. Greater shifts in serum potassium due to a larger gradient may be important in terms of facilitating a greater risk for atrial or ventricular arrhythmia. HD patients within the first three months of starting dialysis have a 30 – 50% risk of either atrial or ventricular arrhythmia. This may be related to large potassium gradients and shifts during and after dialysis.

The treatment options for hyperkalemia in dialysis patients depend on the acuity or chronicity. Acute changes may require dialysis, and of course modification of serum potassium content by shifting it inside cells with glucose or insulin, or raising the threshold for the action potential by administrating intravenous calcium. However, long-term strategies require exercise. In the dialysis patient this would be greater intensity and time on dialysis, as well as perhaps a higher blood flow and lower serum potassium level in the dialysate.

Longer dialysis treatments with higher blood flow are not often possible or acceptable to patients. HD access may be a limiting feature in terms of the amount of blood that can be sent through the dialysis machine, and increasing time on dialysis is often not a popular issue. Thus, strategies for facilitating better long-term control through other means may prove to be important.

Dietary potassium restriction is feasible, but not always possible in every patient; it depends on their food preferences and of course education. Oral binding agents such as sodium polystyrene sulfonate have been available for many years. However, it is associated with poor tolerability and may also cause gastrointestinal necrosis and death. Newer agents such as patiromer and ZS-9 may provide an alternative solution.

Patiromer works by changing calcium for potassium, and it has already been approved for use in the US and the EU A phase III pivotal study, OPAL-HK, demonstrated the importance of patiromer in lowering serum potassium in hyperkalemic non-dialysis patients by about 1 mEq/L. Patiromer has also been studied in a one-year study in patients with chronic kidney disease (CKD), and demonstrated excellent tolerability and no evidence of tachyphylaxis.

There is one HD study with patiromer that was done in six hyperkalemic HD patients, five of whom were anuric. They were studied for 15 days in a general clinical research center, one week on no treatment, and one week on patiromer 12.5 mg daily given in three divided doses. They were not allowed any phosphate binders, and serum and stool samples were collected on a daily basis.

Within one week of patiromer treatment, the percentage of patients with predialysis potassium levels > 5.5, 6.0 or 6.5 mEq/L decreased in a consistent fashion (see table). Overall, patiromer was well tolerated and serum phosphate levels decreased over the course of the week of treatment, perhaps related to the exchange of calcium for potassium with subsequent binding of gut phosphate. Thus, patiromer demonstrated important opportunities to lower both serum potassium and phosphate, likely due to increased fecal potassium and phosphate content. It was well tolerated and there were no discontinuations.

The other potassium binder being studied is ZS-9, also known as sodium zirconium cyclosilicate. It too is effective like patiromer in reducing serum potassium levels in CKD patients. It has not yet been studied in dialysis patients. Unlike patiromer, ZS-9 exchanges sodium for potassium.

In summary, hyperkalemia is common in HD patients. There is the need for improved treatment strategies so that serum potassium levels can be maintained chronically in a safe range. Whether this can be done without increasing dialysis blood flow rates or increasing dialysis time is unknown, but newer oral potassium binding agents may also be helpful. These agents may also prove to be important in reducing large potassium gradients in patients on HD, which, when suddenly changed, may increase the incidence of cardiac arrhythmia.

Exploring the AGEs-RAGE system

Kei Fukami
Kurume, Japan

Diabetic kidney disease (DKD) is one of the most common causes of end-stage renal disease and accounts for the morbidity and mortality in these patients. There is a growing body of evidence that advanced glycation end products (AGEs) and their receptor (RAGE) system play a role in DKD. RAGE is a multi-ligand cell surface receptor that belongs to the immunoglobulin superfamily, which was initially isolated from bovine lung as a binding protein of AGEs.

Binding of AGEs to RAGE activates the PI3K and C1-type domains has been reported to stimulate the generation of reactive oxygen species (ROS) and subsequently enhance various intracellular pathways, such as nuclear factor kappa-B (NF-kB), mitogen-activated protein kinase (MAPK), and protein kinase C (PKC) via the activation of Diaphanous-1, Ras-related C3 botulinum toxin substrate-1 (Rac-1), and cell division cycle 42 (Cdc42) – all of which are associated with the development and progression of DKD.

In humans, RAGE is expressed in podocytes and mesangial cells in the kidneys of diabetic patients with nephropathy. Diabetic RAGE transgenic mice exhibited accelerated glomerulosclerosis compared with their diabetic littermates. RAGE knockout (KO) mice failed to develop the characteristic pathological changes in DKD. These findings suggest that RAGE plays a central role in the progression of diabetic glomerular and interstitial injury.

Recently, we have reported that administration of DNA-aptamer, a short, single-stranded DNA molecule, raised against AGEs (AGEs-aptamer) that can bind with high affinity and specificity to AGEs-modified proteins, inhibits diabetes-induced ROS generation, AGEs accumulation, RAGE expression, and inflammatory changes in the kidney associated with the improvement of albuminuria and glomerulosclerosis in a type 2 diabetic animal. Furthermore, AGEs-aptamer inhibited AGEs-induced oxidative, inflammatory, and fibrotic reactions in cultured mesangial cells by blocking the binding of AGEs to RAGE. Moreover, AGEs-aptamer can improve glycemic control and prevent adipocyte remodeling in fructose-fed rats, partly via suppressing the AGEs-RAGE-mediated oxidative stress generation. In addition, we have recently innovated DNA-aptamer raised against RAGE and found a beneficial effect on the progression of DKD.

A promising therapeutic target for diabetic kidney disease

Session 5.4
Heart failure in chronic kidney disease
Sunday, 15.15 – 16.45, Hall N103 – 104

Session 0.10
ERAA-EDTA & Japanese Society of Nephrology
Sunday, 17.00 – 18.30, Hall 10B
TREATMENT ADVANCES TO THE PATHWAY OF ELIMINATION OF CHRONIC HCV INFECTION IN CKD PATIENTS

Learn more about the burden of chronic HCV infection in patients with renal impairment at the MSD Symposium

SUNDAY, 4 JUNE 2017 • 13:40 – 14:50 • Room N117-118

CHAIR
Jose M. Morales
Professor of Medicine
Consultant Investigator in the Research Institute of Hospital Madrid Transplantation Society
Madrid, Spain

Kosh Agarwal
Institute for Liver Studies
King's College Hospital
London, UK

Niraj Desai
Assistant Professor of Surgery
Transplant Division
Johns Hopkins University
Baltimore, Maryland, USA

Michel Jadoul
Head, Department of Nephrology
Cliniques Universitaires Saint-Luc
Université Catholique de Louvain
Brussels, Belgium

FACULTY

Hemodialysis patients with HCV are at an increased risk of mortality and morbidity compared to those without HCV.1

LEADERSHIP • COMMITMENT • INNOVATION
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Two major issues have prevented the wider use of blood flow.

Citrate has many characteristics of the ideal anticoagulant for hemodialysis. Its anticoagulant effect (mediated through depletion of Ca++) is immediate, complete and limited to the dialysis circuit. Citrate has a very specific antitoxin: calcium. In addition to inhibiting coagulation, citrate reduces platelet deposition on the dialyzer membrane. The dialyzer membrane exchanged with a scanning electron microscope showed negligible thrombus formation after regional citrate anticoagulation. In contrast, pronounced cell adhesion and thrombus formation were demonstrated after standard heparin or nadropramine anticoagulation.

By chelating calcium and magnesium, citrate may reduce complement activation induced by the interaction of blood with the artificial membrane, thus improving the biocompatibility of the dialysis circuit. Unlike heparin, citrate has no antitoxicity. Citrate is easily dialyzable (molecular weight 100 g/mol), with more than 80% removal through the high-flux membrane. The cost of citrate is low.

Two major issues have prevented the wider use of regional citrate anticoagulation (RCA) in the past: the risk of metabolic complications and the complexity of the RCA procedure with safety concerns. Today the risk of metabolic complications (alkalosis, acidosis, hypo- or hypercalce mia, hypernatremia) is greatly reduced by the use of high-flux dialyzers with high citrate clearance, adjustment of sodium and bicarbonate offered by modern hemodialysis monitors, and wide availability of point-of-care ionometers. The latter, together with good protocols and availability of precise infusion pumps, reduce the complexity of the procedure.

RCA during intermittent hemodialysis is usually performed using calcium-free dialysate, trisodium-citrate infusion (as close to the patient as possible), and calcium infusion just before the dialysis is renewed (or pre-dialyzer) ionized calcium level, targeted to 0.3–0.4 mmol/l. This level of ionized calcium is enough to prevent clotting. With higher hemocitocrit, lower citrate doses are needed.

Post-dialysis ionized calcium level is lower than pre-dialysis because of the calcium efflux from the plasma dialyzed against calcium-free dialysate. Of course, it is vital to replace calcium before hypocalcemic blood is returned to the patient. Maintaining normal ionized calcium in the patient's blood is the most important safety issue in RCA. The use of calcium-containing dialysate during RCA could have the advantage of simplifying the procedure and increasing safety, but the trade-off is increased clotting in the dialysis circuit.

RCA is well established in the field of acute kidney injury. All modern continuous renal replacement therapy (CRRT) monitors provide automated RCA as a standard procedure. KDIGO guidelines for CRRT suggest using RCA rather than heparin, regardless of the risk of bleeding. Although citrate modules are not available for intermittent hemodialysis, RCA is expanding. Good protocols, trained nurses, wide availability of infusion pumps and point-of-care ionometers, and familiarity with RCA from CRRT have all contributed to this expansion. Safe RCA use has been demonstrated in pediatric high-flux hemodialysis, single-needle hemodialysis, on-line hemofiltration and hemofiltration. Long-term RCA in selected patients, performed for years, is a clinical reality.

Nurses’ acceptance of RCA was a critical issue in its expansion in Slovenia in the early 1990s. Despite all the technical complexities, nurses pre-ferred citrate to heparin-free dialysis with saline flushes (the main option for patients at risk of bleeding before introduction of citrate). The major reason was a perfectly ‘clean’ dialysis circuit after dialysis, usually without any clots. Dialyzer and bloodlines after hemodialysis with RCA often looked as if they had not been used. This was achieved in parallel with patient safety and acceptable procedure complexity.

In 2016, more than 12,000 RCA procedures (>1000 per month, >20 per day) were performed by our Centre for Acute and Complicated Dialysis at University Medical Centre Ljubljana. RCA hemodialysis is routinely performed at other in-hospital Slovenian dialysist centers, and at some free-standing hemodialysis units.

As an anticoagulant, citrate has many advantages over heparin in hemodialysis.

In conclusion, citrate has many advantages over heparin as an anticoagulant in hemodialysis. Although the citrate module is not (yet) routinely available for intermittent hemodialysis (as it is for CRRT), strict protocols, trained nurses, precise infusion pumps, point-of-care ionometers and high citrate clearance in high-flux dialyzers all guarantee the safety of the procedure, with minimal risk of metabolic complications. This allows for the expansion of RCA in intermittent hemodialysis, and the exploration of potential beneficial effects of citrate beyond anticoagulation.

References

Cappuccino with Claudio Ronco
Take a break and enjoy a cappuccino while watching a video of Professor Claudio Ronco on www.youtube.com

The attendees of the 54th ERA-EDTA Congress are invited to join his “Cappuccino with Claudio Ronco” series on Youtube (enter “Cappuccino with Claudio Ronco” into the search mask on Youtube). In his short films Professor Ronco discusses new topics with other experts.

Fresh videos will be available tonight!
Citrate anticoagulation: first-choice anticoagulant in CRRT

HELEEN M. OUDEMANS-VAN STRAATEN
Amsterdam, The Netherlands

When blood enters the renal replacement circuit, anticoagulation is required to prevent clotting. Heparin is the common anticoagulant, but heparin also causes systemic anticoagulation. In contrast, citrate provides regional anticoagulation and does not increase the patient’s risk of bleeding.

Citrate: anticoagulant
Citrate acts as an anticoagulant by chelating ionized calcium (iCa), a necessary cofactor for clotting, and inducing hypocalcemia in the filter. At an iCa concentration below 0.25 mmol/L, anticoagulation is maximal. Citrate is partially removed by dialysis/filtration, the remains enter the systemic circulation where it is rapidly metabolized in the mitochondria of liver, muscle and kidney. The chelated calcium is released. The amount of calcium lost via the filter is replaced adjusted to iCa concentrations in the patient’s blood. [1,2]

Citrate: buffer base
Because sodium citrate is also a buffer, citrate anticoagulation requires fluids with an adjusted buffer content. Different citrate modalities are available. Modern continuous renal replacement therapy (CRRT) devices have an algorithm incorporated requiring dedicated fluids. The buffer strength of sodium citrate is equivalent to 3 mmol bicarbonate per mmol citrate if all cations are sodium (trisodium citrate), and less so if part of the cations are hydrogen (citric acid) as is sometimes the case. [1,2] Thus, while the anticoagulant strength of the citrate solution depends on the citrate concentration in the filter and citrate dose is adjusted to blood flow, the buffer strength depends on the citrate cation. [1,2] Although the dual action of citrate and its consequences are difficult to understand, daily practice is simplified by the use of algorithms and their accompanying fluids, which form an all-in-one package. Each protocol has strict rules for metabolic adjustments and requires strict adherence.

The main challenges are implementation and to convince colleagues of its benefits

Citrate: clinical benefits
Despite its theoretical complexity, the latest meta-analysis comparing citrate to heparin concluded that regional citrate is more efficacious in prolonging circuit lifespan and reducing the risk of bleeding than heparin, and should be first-choice anticoagulant for critically ill patients who require CRRT. [3]

Citrate accumulation
The safe use of citrate is limited by its metabolism in the mitochondria of liver, kidney and muscle. When citrate is not metabolized, it accumulates and lowers systemic iCa concentration. A rise in total/iCa ratio above 2.5 is the most specific warning sign. Because citrate is not metabolized and sodium citrate is not used as buffer base, metabolic acidosis ensues. Risk factors are severe systemic hypoperfusion (because mitochondrial metabolism is oxygen dependent) and decompenated liver cirrhosis. [1,2]

Monitoring and consequences
Monitoring of citrate anticoagulation includes the measurement iCa, total Ca, total/iCa ratio, Na+ and acid base balance in systemic blood. Low iCa may be due to insufficient calcium supplementation, in which case total calcium is also low. The calcium supplementation rate should be increased according to the protocol. Low iCa may also be caused by citrate accumulation, in that case total Ca rises and the total/iCa ratio also rises.

In case of severe metabolic failure, metabolic acidosis develops and lactate concentration is high due to the underlying condition, e.g., severe tissue hypoperfusion or decompenated liver cirrhosis. If metabolic acidosis occurs, the administration of citrate is discontinued and bicarbonate buffered solutions are used. Calcium is administered, because hypocalcemia can contribute to hypotension. It should, however, be noted that the occurrence of citrate accumulation is a sign of severe disease. In several studies a mortality rate of 100% is reported, related to the underlying disease.

Finally, metabolic acidosis or alkalosis may be due to too much or insufficient buffer supply. Subsequent actions depend on the protocol. In principle, more buffer can be given by increasing citrate infusion rate or using additional bicarbonate supplementation, vice versa. However, each protocol has specific guidelines for correcting derangements and nurses should stick to the protocol.

Challenges
Since citrate is the first-choice anticoagulant for CRRT, the main challenges are to take the decision to implement citrate anticoagulation in the unit and convince colleagues and nursing staff of its benefits. Nurses in particular support citrate, because they do not like a bleeding patient or a clotted circuit. Second, the unit chooses the modality (hemodialysis or hemofiltration) and the device. None of the modalities has proven superiority on clinical endpoints. Third, a training program is initiated. A very important aspect is to create alertness with the nurse to check iCa and acid base status, to adjust calcium supplementation, detect citrate accumulation and to protocolize the necessary steps. In the end, all stakeholders of CRRT will be grateful, because CRRT will bring less bleeding and longer circuit life, and can be performed without additional hazards in patients at risk of bleeding.

References

Session 5.6
Hemodialysis anticoagulation: present and future
Sunday, 17.00 – 18.30, Hall N105 – 106
Citrate in dialysate – The standard for the next decade in hemodialysis?

MICHAEL SCHMITZ
Solingen, Germany

The primary buffer substance that is supplied to the patient in the context of hemodialysis treatment is bicarbonate. However, since calcium and magnesium must also be added to the dialysate, these two components cannot be stored together in a concentrated solution without precipitating in the form of sparingly soluble calcium and magnesium carbonate. Therefore bicarbonate is mixed with the dialysis concentrate and pure water within the dialysis machine. In addition, the concentrate contains a small amount of a salt of a weak acid, usually acetate, which can to a certain extent prevent precipitation of calcium carbonate.

The idea of using citrate as a component in the dialysate is less based on its anticoagulative property, than on its greater biocompatibility compared to the otherwise used acetate. The concentration of citrate in the dialysate of about 1 mmol/L is clearly below the 3–4 mmol/L that is necessary to reduce ionized calcium to a level sufficient for anticoagulation. However, local anticoagulatory effects are seen that can also contribute to a more effective dialysis. It is also suggested that the indirect citrate buffer can help to control uraemic acidosis due to the slow metabolism of citrate to bicarbonate. In addition, acetate in higher concentration causes hypotension, nausea, vomiting, headache and angina pectoris. The low concentrations usually used in hemodialysis are also considered potentially dangerous for hypotonic patients.

The safety of a citrate-containing dialysate in various dialysis forms (hemodialysis, pre- and post-dialysisfiltration) was demonstrated in a prospective, randomized study including 92 patients. [1] The observed mild side effects (especially cramps), which only occurred during the first two weeks of therapy, can be explained by the fact that when a citrate-containing dialysate is used, a calcium concentration of approximately 0.2 mmol/L higher than the corresponding acetate solution is required in order to obtain a comparable net calcium supply. An advantage was that post-dialysis alkalosis was significantly less frequent, similar to a study by Nunez. [2] In the latter study, less inflammation and dialysis efficiency was also observed. Other authors report an increased biocompatibility, [3,4] however, many authors report a slight postdialytic calcium drop of about 0.1 mmol/L with consecutive increases in iPTH. The clinical significance of this observation is still unclear. A recently published study showed for the first time that dialysis patients who were older than 70 years and were never exposed to acetate dialysate showed a significantly improved survival (HR 0.79). [5] Unfortunately, in this study other techniques of anticoagulation, dialysate and heparin reduction procedures were found similar to regional citrate dialysis. [6]

In conclusion, when used as part of the effort of improving biocompatibility of the hemodialysis procedure, citrate in the dialysate is a safe and well-tolerated option with potential benefits for patients that have to be determined by larger randomized studies. Its particular role in heparin-free dialysis has yet to be defined.

References
Accurate risk prediction for kidney failure can help physicians deliver risk-based care by allowing timely referral to nephrologists, and appropriate planning for dialysis and transplantation. In 2011, we developed the Kidney Failure Risk Equations (KFREs) to predict the need for dialysis and transplant in the next five years in patients with chronic kidney disease (CKD). Since that time, we have extensively validated the KFREs and proven their accuracy in geography, ethnically and etiologically diverse patient populations.

We believe the timing is now right to implement the KFREs in clinical practice, and will present thresholds of 20% over 2 years as criteria for initiating dialysis and transplant in the next five years as a way to begin applying the best validated risk scores and further research in predictive modeling for kidney failure should focus on implementation rather than new development and validation. Implementation research through cluster randomized trials, and observational studies pre/post quality improvement interventions that include the KFRE can translate this knowledge to action.

The two polar-reviews on predictive models by Dr Tangri and Dr Dekker will test their potential usefulness in CKD patients in diverse clinical situations and geographical areas.

“Prediction is very difficult, especially if it’s about the future”. This famous quote attributed to quantum physicist and Nobel Prize winner Niels Bohr has lost nothing of its power since the last century. While developing prediction models has become quite popular both in nephrology and in medicine in general, most models have not been implemented in clinical practice on a larger scale. This should be no surprise, as the majority of published models has been shown to be poorly reported and often developed using inappropriate methods. Main problems identified relate to either using too few candidate predictors (based on univariable p<0.05) or too many (for the number of events), resulting in poorly performing prediction models. In addition, many people are incorrectly inclined to interpret variables in a prediction model as being causal.

Guidelines on how to develop and test a prediction model all stress the importance of external validation to test discrimination and calibration in other populations, as usually prediction models perform less well in new subjects. However, external validity has not often been tested for prediction models in renal patients. Moreover, impact studies showing improved clinical outcomes when using a prediction model in routine clinical practice have been reported rarely.

By and large, notwithstanding a few notable exceptions like the KFRE prediction model developed by Tangri and colleagues, most models have not been validated externally or are at best inadequately reported, preventing them to be used in clinical practice. Therefore, we recommend researchers to spend more energy on validation and assessing the impact of existing models, instead of merely developing more models that will most likely never be used in clinical practice.

References
After the disaster: an overview of treatment of crush syndrome

Literally, crush means ‘injury due to pressure between opposing elements’. Crush syndrome (CS) describes the systemic manifestations of crush injury-induced rhabdomyolysis. These manifestations include surgical and medical findings. The most important surgical feature in CS is the compartment syndrome. Medical features include, but are not limited to, hypovolemic shock, hyperkalemia, infections and acute kidney injury (AKI).

The most important therapeutic intervention is early volume resuscitation

The underlying pathology in CS is rhabdomyolysis. Pathogenesis of rhabdomyolysis-induced AKI is multifactorial; the most important mechanism is volume depletion mainly due to dramatic fluid third-spacing. This may cause renal hyperperfusion, isometric damage and acute tubular necrosis. Myoglobinuria, and several other factors also contribute to the pathogenesis.

Mortality in disaster crush victims is around 15–20%. Therefore, emergent treatment is necessary to improve prognosis. Therapeutic interventions should be considered separately at the disaster field, during transportation and at admission to hospital. The extent of all these interventions varies according to availability of material and personnel sources in disaster circumstances. Overall, the most important therapeutic intervention is early volume resuscitation for the prevention of crush-related AKI. If this is not successful, dialysis is vital for the treatment of established AKI.

When considering prevention, the question is: what type of fluids should be used in these cases? Colloids can be used, but they have no major benefit on morbidity and mortality, a higher risk of side effects such as anaphylaxis or coagulation abnormalities, a risk of tubular injury at high doses (starch preparations), and higher costs. Therefore, colloids should not be preferred in crush-related AKI.

Although bicarbonate solutions are useful in reducing acidosis and hyperkalemia, their preparation may be complicated in mass disasters. Excessive alkalinization also has drawbacks, such as the promotion of symptomatic alkalosis and worsening of hypocalcemia. Therefore, isotonical saline, a readily available solution in disaster conditions with easily managed side effects, should be preferred.

There are other targets in fluid resuscitation that can be accomplished by means of mannitol administration. Mannitol may expand plasma volume, has diuretic, antioxidant and vasodilatory effects, and also decreases muscle intracompartmental pressure. However, it has some important side effects (congestive heart failure in case of overdose, and potential nephrotoxicity), and there are inconsistent reports on its efficacy in traumatic rhabdomyolysis. Mannitol is also contraindicated in anuric patients.

Timing and volume are probably more important than the type of fluids. Treatment should be initiated as soon as possible, ideally even when the victims are still buried under the rubble. Before rescue, an infusion rate of 1 L/hr for adults (15–20 ml/kg of body weight per hour for children) is appropriate in most victims. Fluids should be continued both during and after extrication. Generally 3–6 L of fluid are given initially taking into account many variables. Later, the amount of fluid should be determined according to urine response and logistic circumstances. This protocol is subject to change depending on many variables, including age, body weight, trauma pattern, duration of extrication, urine production and amount of overall estimated fluid loss by the victim, as well as ambient temperature and logistic circumstances.

Since crush-related AKI is a highly catabolic disorder, dialysis is frequently needed. So the question is: when to dialyze? The standard clinical and biochemical indications for dialysis are also valid for these patients. Importantly, since hyperkalemia is very frequent and life threatening, prophylactic dialysis (dialyzing patients even before the appearance of traditional indications) must be considered. In KDIGO AKI guidelines, this issue has been emphasized by the advice to “consider the trends of laboratory tests, rather than single BUN and creatinine thresholds alone”.

All dialysis modalities have both medical and logistic advantages and drawbacks. Overall, intermittent hemodialysis (HD) is the best dialysis option in crush victims. In the Marma- ra earthquake experience, 477 of the 639 crush patients needed renal replacement therapy, and a total of 5137 HD sessions of HD were performed when treating these cases. This experience has been highlighted as the largest dialytic intervention in AKI patients in the literature.

Finally, the question is: when to transfer a CS patient to an intensive care unit (ICU)? Since CS is a fatal disorder, transfer to ICU should be considered in patients with any life-threatening complication. These include thoracic and/or abdominal trauma or acute respiratory distress syndrome and disseminated intravascular coagulation, all of which are important predictors of mortality in crush victims. On the other hand, one should be very cautious and selective when defining the indications after mass disaster because of shortage of ICU positions in these circumstances. Namely, ICU beds should be reserved for the most critically ill patients who have a high probability of survival.

To conclude, crush-related AKI is a frequent major cause of death in routine clinical practice and after earthquakes. Management of these patients may differ considerably because of medical and logistic circumstances. Finally, deaths due to crush-related AKI can be reduced by appropriate medical and logistic management.

References

Direct antivirals: a new era in HCV eradication

Infection with the hepatitis C virus (HCV) affects 185 million people worldwide. After an acute infection 80–85% of patients develop a chronic infection. Liver-related complications such as cirrhosis, reaching 40% after 30 years of chronic infection, and an increased risk for hepatocellular carcinoma are well known. It has, however, become evident that HCV is also associated with extraneoplastic complications, including chronic kidney disease (CKD).

HCV is associated with reduced survival in dialysis and has also repeatedly been shown to increase the risk of death and graft loss after kidney transplantation. Liver disease plays a role, but cardiovascular disease and infections are also important contributors to increased mortality. Transplanted patients are at risk of developing HCV-associated relapsing or new-onset glomerulonephritis. Post-transplant diabetes is also a substantial problem.

HCV eradication has therefore been recommended before kidney transplantation. However, the interferon-based (IFN) therapies combined with ribavirin have achieved only 40–50% cure rates and have been especially cumbersome in the dialysis population. In transplanted patients, IFN has been contraindicated due to an increased risk of rejection. Of the 49,762 hemodialysis (HD) patients included in the international Dialysis

Outcomes and Practice Patterns (DOPPS) study, 9.5% were HCV+, but only 1% of 4,589 patients with prescription data and 3.7% of waitlisted patients were receiving antiviral medication.

Fixed-dose direct antiviral (DAA) combinations, such as elbasvir-grazoprevir, ledipasvir-sofosbuvir, and paritaprevir-ombitasvir-ritonavir (with or without ribavirin), have achieved sustained virologic response rates (SVR; undetectable viral load 12 weeks after completing therapy) of >95–95% in most patients. With the exception of sofosbuvir, these drugs are cleared by the liver.

The standard of care for treating HCV has also been changing rapidly in KDOP at the last few years, with several IFN-free options approved or in phase 3 studies. C-SURFER, the largest study, randomized 224 DOK 4 or 5 patients (including HD) with HCV genotype 1 to receive either immediate treatment with elbasvir-grazoprevir or...
Hyperkalaemia in CKD: An Evolving Treatment Landscape

Learning objectives

The objectives of this educational event are to help delegates understand:

1. The burden of illness of hyperkalaemia in patients with chronic kidney disease (CKD)
2. The risk of cardiac abnormalities and mortality that hyperkalaemia gives rise to in patients with CKD, and how these can be managed
3. The potential of current and investigative therapies to maintain normokalaemia in patients with renal disease

Agenda

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<td>Hyperkalaemia and Its Role in Cardiac Outcomes in Patients with CKD</td>
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Good news for YNP members: A new partnership begins with the ASN

Once more, the ERA-EDTA ‘Young Nephrologists’ Platform (YNP) has good news for its members. Starting in 2017, YNP, under the umbrella of the ERA-EDTA, will begin a partnership with the American Society of Nephrology (ASN): the Young Nephrologist Speaker Exchange project. Each year, a member of YNP will be invited by ASN to present at the ASN Congress, specifically at the YNP Session.

For 2017, it is our pleasure to announce that Dr Gentzon Hall will be invited, as our young ASN guest at the YNP Session. The topic of his lecture will be “Mining the therapeutic potential of novel discoveries in renal genetics”. Furthermore, we are pleased that Dr Rafael Kramann, YNP member since 2014, was chosen by ASN to be present at ASN Kidney Week in New Orleans, USA, from 31 October to 5 November 2017. If you are a YNP Member and would like to speak at the ASN Congress, we suggest you follow our e-newsletters closely. Every year we will ask for candidates from our members in order to select and suggest two names for the exchange project, after which ASN will choose one member.

If you are not yet a YNP Member and are younger than 40 years of age, we invite you to apply for YNP membership on the ERA-EDTA website: www.era-edta.org/membership/ynp_registration.php.

deferred treatment. [2] The final results demonstrated an SVR of > 98 % in both study arms. [3]

ERA-EDTA has in a recent statement described patients with CKD stages 4–5 as a priority group for DAA treatment. However, in my opinion, treatment focus in CKD should not only be on CKD 4–5 and transplantation. Most cases of HCV-associated kidney disease will be cured with DAs. Furthermore successful HCV therapy may contribute to a reduced ESRD and CVD risk in CKD. For diabetic patients with HCV there may be an even stronger protective effect.

Nephrologists must be involved in decisions about patient selection for treatment

At this meeting, data are presented regarding cumulative survival for HCV patients on HD grouped on ever-receiving IFNa-based HCV or not (n=42 versus 223). Sixty percent of patients were treated on HD, 40 % had received treatment prior to dialysis therapy. After controlling for age, kidney transplantation and acute kidney failure in a multivariate regression analysis, the risk of dying in patients who had never received HCV treatment remained significant-ly higher (Figure 1). The reason is not clear, but may reflect cumulative cardiovascular effects of the combination of ESRD and HCV and other comorbidities. These results suggest that antiviral treatment before or during HD may confer better survival for patients waitlisted for transplantation (Bruchfeld et al, SP 305).

To conclude, HCV is the first chronic viral infection that may be cured in most patients including CKD. New updated KDIGO HCV guidelines will soon be available. Nephrologists must become aware of the potential benefits for renal patients of HCV eradication, and also involved in decisions about patient selection for DAA therapy.

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If you are not yet a YNP Member and are younger than 40 years of age, we invite you to apply for YNP membership on the ERA-EDTA website: www.era-edta.org/membership/ynp_registration.php.
Organoid models and applications in biomedical research

The use of stem cells offers significant prospects for research and therapy. Currently, several cell types can be generated in vitro, due to methodological advances in isolating and handling cells from various tissues and, even more importantly, because cell identity can now be changed by reprogramming and re-differentiation.

Organoids are usually generated from progenitor cells, which are either isolated from embryos or derived from pluripotent stem cells (PSCs) (Fig. 1). These methods evolved, methodologically and conceptually, from classical reaggregation experiments that demonstrated that dissociated cells from embryonic organs can re-aggregate to re-form the original organ structure. Most organoid technologies are based on the use of exogenous growth factors that drive particular cell identities, as well as extracellular matrices, followed by reaggregation to stimulate cell movement and create self-organized 3D tissues.

As has been shown for other organs, evidence that kidney tissue may be capable of self-organization comes from early reaggregation experiments [1], and recent studies have confirmed that kidney organoids can be obtained from various sources of progenitor or stem cells. Using a suspension of embryonic mouse cells, we recently generated kidney tissues that were able to filter blood in vivo, reabsorb macromolecules, and produce erythropoietin [2]. Building on this, we then constructed renal organoids using human amniotic fluid stem cells that vascularized upon transplantation, formed highly specialized human podocytes, and exerted nephron-specific functions [3]. Most importantly, the generation of kidney organoids, starting with human induced PSCs [4, 5], has created significant opportunities for investigating organ development and tissue morphogenesis, modeling diseases, testing the efficacy and toxicity of drug compounds, and hopefully one day for creating tissues for tissue replacement therapy.

In this lecture, we will outline historical advances in the field and describe some of the major recent developments in 3D organoid formation, with a special emphasis on progress with generating kidney organoids. Finally, we will underline current limitations and highlight examples of how organoid technology can be applied in biomedical research.

Figure 1: Human Amniotic Fluid Stem Cells incorporate in mouse organoids (a) and generate functional podocytes (b) capable of internalizing exogenously infused BSA when the organoid is transplanted under the renal capsules of rats. Xinaris et al. J Am Soc Nephrol 2016; 27(5): 1400-11. By courtesy of the American Society of Nephrology.


References
Do biomarkers have a clinical utility for disease progression of CKD?

Chronic kidney disease (CKD) affects more than one out of 10 adults in industrialized countries. Of note, the vast majority of affected individuals have mild to moderate CKD, and only a few patients require renal replacement therapy (RRT). According to traditional assumptions, CKD is a progressive disease, which starts with only minor impairment in renal function and eventually advances towards severe disease stages that will ultimately require RRT to prevent death from uremia. However, recent large-scale epidemiologic analyses failed to prove such a uniform disease pattern. Instead, CKD progression is highly heterogeneous, with some patients fast advancing towards dialysis dependence, while renal function remains stable over years in others.

An unmet clinical challenge in nephrology is to distinguish between patients whose CKD will be stable for the foreseeable future and those in whom CKD will progress. Early identification of high-risk patients would allow us to focus on protective treatment upon subjects who are most likely to benefit. Vice versa, patients at low risk of CKD progression may be relieved of a burden when they learn that they are unlikely to require RRT, and the need for nephrology visits and pharmacotherapy may be relaxed in these patients.

In addition, identification of patients at high-risk of progression may enrich future randomized trials on CKD progression and so reduce the study population of such trials. This is in the context of repeated claims by stakeholders that there is a dire need for novel preventive options in clinical nephrology, when pharmaceutical companies are rather reluctant to develop new treatment strategies after the recent failure of several innovative drugs.

At the same time, KDIGO guidelines advocate the identification of CKD patients at higher risk of rapid progression. Unfortunately, risk prediction remains to date underdeveloped in clinical nephrology, even though easy-to-use tools have been made available in the last decade. The simplest approach has been incorporated into KDIGO guidelines; it uses estimated glomerular filtration rate (eGFR) and albuminuria categories to distinguish patients at low, increased, high and very high risk for CKD progression. Nevertheless, such an approach will be of limited precision, since the continuous variables eGFR and albuminuria are transferred into categorical parameters, by which they partly lose their predictive power. This may be illustrated by the example of two 50-year-old female CKD patients, one of whom has an eGFR of 59 ml/min/1.73 m² and albuminuria of 301 mg/g creatinine, and the other has eGFR of 45 ml/min/1.73 m² and albuminuria of 7500 mg/g creatinine. According to KDFGO, both women would be attributed to the ‘very high risk’ category.

Thus, the development of the Kidney Failure Risk Equation (KFRE), which incorporates eGFR and albuminuria as continuous variables, along with age and sex, was a major step forward. In the above example, the two women at ‘very high risk’ for CKD progression would have a 5-year risk for end-stage renal disease of 0.89 % and 16.73 %, respectively.

The KFRE was originally developed in Canada, but has since been globally validated in numerous cohorts. Notably, its discriminatory power for predicting CKD progression is stronger than the power of conventional cardiologic risk equations that aim to predict atherosclerotic cardiovascular events, such as the Framingham Risk Score. The conventional approach to measure discriminatory power is the c-statistic, which yields a numerical value between 0.5 (equal to a coin toss) and 1.0 (equal to perfect discrimination). In several independent validation cohorts, the KFRE reached a c-statistic close to 0.9, while cardiovascular risk equations generally yield c-statistics below 0.8.

This high discriminatory power of the KFRE sets the bar high for novel predictors of CKD progression. Many novel markers that are very impressive in univariate Kaplan-Meier analyses fail to provide independent prognostic information once they become attributed to eGFR, albuminuria, sex and age, or directly integrated into the KFRE. This may be illustrated by the example of ultrasound renal resistive indices (RI), which have been claimed for years to predict CKD progression among nephrology patients. In our CARE FOR HDw study, we demonstrated that the predictive power of RRI was substantially attenuated once we adjusted for the components of KFRE. Similar findings were recently reported for urinary biomarkers of tubular injury within the CRIC cohorts. To our best knowledge, no biomarker so far has been shown to improve prediction of CKD progression beyond the KFRE.

In summary, CKD progression is highly heterogeneous. For the time being, clinical nephrologists should focus on the KFRE for risk prediction. Epidemiologists may go ahead and attempt to further improve prognostic tools by integrating novel biomarkers into the KFRE. Finally, clinical scientists should design prospective studies to test the hypothesis that focusing on renoprotective prevention and treatment strategies upon patients at highest risk for CKD progression will delay need for RRT among these individuals, without putting low-risk patients at risk of undertreatment.
Accelerated aging and chronic inflammation in CKD

Patients with end-stage renal disease (ESRD) experience complications in various organ systems that resemble an accelerated aging process. These include increased vascular stiffness, atherosclerosis and vascular calcifications (which may be aptly termed ‘vascular progeria’), a decrease in lean tissue mass and muscular strength, osteopenia and reduced cognitive function. Senescence of the adaptive immune system has also been observed. As a final common pathway, these changes may contribute to the frailty syndrome, which may be present at a young age in ESRD patients and is associated with a greatly increased mortality risk. These complications already occur, albeit in a milder form, at earlier stages of chronic kidney disease (CKD). At a cellular level, there is also evidence of accelerated aging, as exemplified by a reduction in telomere length as compared to age-matched healthy subjects.

Various mechanisms likely contribute to this process, such as an increase in oxidative stress and sympathetic nerve activity, accumulation of pro-aging factors (phosphate and advanced glycation end products), as well as a reduction in anti-aging proteins, such as Klotho. However, evidence connecting underlying mechanisms with cellular abnormalities and, subsequently, with the premature aging phenotype in uremic patients is still limited.

Arguably, one of the most important contributing factors to an accelerated aging process in uremia is systemic inflammation. This is characterized by an activation of the innate immune system and is evidenced by an increase in inflammatory mediators such as C-reactive protein, interleukin-6 and TNF-α. As shown in Figure 1, systemic inflammation in uremia has several possible causes. Whereas dialysis therapy itself certainly contributes to systemic inflammation, various causes directly related to renal failure are also involved, such as fluid overload and accumulation of protein-bound toxins.

Several mechanisms link chronic inflammation to accelerated aging in uremia, both in relation to cellular abnormalities such as telomere shortening, as well as to its phenotype. Uremic inflammation is related to vascular progeria, as well as to a loss of lean body mass and osteopenia, and possibly also to cognitive impairment. At a mechanistic level, inflammation leads to a reduction in anabolic pathways and a stimulation of catabolic pathways, which are involved in muscle wasting (Figure 2). Inflammatory mediators also directly induce calcification of vascular smooth muscle cells in combination with abnormalities in mineral metabolism. Chronic activation of the innate immune system in a non-uremic model also induced telomere shortening as well as a premature aging phenotype, providing evidence for a direct link between inflammation and the aging process.

There is an intriguing relationship between inflammation and Klotho. On the one hand, the anti-aging properties of Klotho may be related to inhibition of the inflammatory master regulator NF-κB. On the other hand, inflammatory cytokines in turn downregulate Klotho gene expression, thus providing a direct and reciprocal link between inflammation and aging. Interestingly, cellular senescence, in the form of the senescence-associated secretory phenotype (SASP), may itself be a contributing factor to systemic inflammation. Evidence for the relevance of the SASP in renal disease is still limited, although recent evidence linked vascular senescence with an inflammatory phenotype in vessels of uremic patients.

The concept of premature aging is not unique to uremia, but has also been observed in other chronic diseases such as chronic obstructive pulmonary disease (COPD), rheumatoid arthritis, and HIV. Comparable phenotypic changes, such as premature atherosclerosis, sarcopenia, osteopenia and cognitive impairment are observed in all these diseases. Also an increase in vascular calcification, though not as pronounced as in CKD, has been observed in COPD and HIV, as well as in rheumatoid arthritis. In addition, in COPD and CKD, senescent cells in respectively lung and kidney epithelial cells have been observed, suggesting that an accelerated aging process also plays a role in the further deterioration of the primary affected organ. Another argument for a role of aging in these chronic debilitating diseases is telomere shortening and senescence of the adaptive immune system.

As holds true for CKD, all the above-mentioned diseases are characterized by systemic inflammation, albeit with different causes. In COPD and rheumatoid arthritis, spillover of mediators from the lung and affected joints are major culprits, whereas in HIV mitochondrial damage and oxidative stress due to antiretroviral therapy may be a major contributing factor. Apart from the disease-specific causes, lifestyle changes such as physical inactivity and smoking are also related to systemic inflammation.

Thus, despite major differences in causality, it is likely that systemic inflammation is an important final common pathway in different chronic diseases. This contributes to an accelerated aging process with, at least in part, comparable phenotypes between chronic inflammatory diseases. Interestingly, other factors related to aging, which were thought to be more specific for uremia, such as reduced Klotho expression and accumulation of advanced glycation end products, have also been observed in HIV, COPD and rheumatoid arthritis. The same could conversely hold true for deficiencies in anti-aging factors, which have been well studied in COPD but less so in CKD, such as members of the sirtuin family that are potentially amendable to pharmaceutical intervention.

Does the accelerated aging concept have any relevance? I believe a positive answer can be given to this question because it may open a new area of research that broadens our view beyond the organ-specific domain. By identifying shared mechanisms between chronic diseases and learning from the rapidly evolving field of geroscience, in future a wide range of possible therapeutic opportunities could be opened that may be relevant for the systemic complications of CKD.

References

Figure 1: Causes of uremic inflammation © Kooman

Figure 2: Inflammation in relation to premature aging © Kooman

View the ERA-EDTA 2017 Broadcast on the YouTube playlist here.
**What’s on in Madrid?**

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| Mercadillo del Gato                        | The Mercadillo del Gato is once more opening its doors, where over 60 exhibitors from different origins will offer select products related to fashion, handcrafts, gourmet food, decoration, accessories, cosmetics, jewellery and collecting. The Westin Palace  
Today, 11.00 am – 9.00 pm |
| Pity and Terror in Picasso. The Path to Guernica | On the occasion of the 80th anniversary of the first time Guernica was shown, this exhibition deals with Picasso’s view of modern war, as shown by his imagery of agony, perplexity, and horror. Reina Sofia Museum  
Today, 10.00 am – 7.00 pm |
| Rayo Vallecano – Córdoba CF                | On the last game home this season, Rayo Vallecano and their supporters hope they can go back to the highest level of Spanish football. The Vallecas-based team are playing home against one of the most powerful squads in second division. Rayo Vallecano Stadium  
Today, 8.00 pm |
| Corral de la Morería                       | This is one of the oldest tablaos in the capital and opened in 1956. It is regarded by many as the cathedral of Flamenco art in Spain. This is one hotspot in Madrid nightlife that you can’t afford to miss. Calle Morería, 17 28005  
Today, 7.00 pm – 1.30 am |
| Guns n’ Roses                             | One of the most legendary hard rock bands are coming back to Madrid on their “Not In This Lifetime Tour.” Guns N’ Roses are back together with award-winning lead guitarist ‘Slash’ after more than two decades. Vicente Calderón Stadium  
Today, 8.00 pm |
| 400th Anniversary of Madrid’s Plaza Mayor | Today: The Andante Company. The diverse programme includes new circus, object theatre, humour, music and dance, among other shows, and turns Madrid into a stage that will take the audience through surprising and unexpected shows. Plaza Mayor  
All day |

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In ‘Difficult patient or wrong communication?’, the first-ever interactive role-play workshop at an ERA-EDTA Congress, Professor Wim Van Biesen (Belgium) joined two professional actors to demonstrate techniques to improve communication with patients. Professor Van Biesen said: “Patients of course expect professionalism from their healthcare workers, but this is not the major factor for them. What they really want is for us to be responsive to their needs with compassion and empathy, and empower them to take decisions about their care.” International guidelines state that good patient care involves listening to patients, informing them of their choices, and involving them in shared decision making. In a second part of the session titled ‘Shared decision making with patients: opportunities and pitfalls’, Professor Van Biesen and the actors, again with contributions from delegates, presented vivid scenarios to show how to optimise shared decision making in nephrology. These highly interactive workshops represent a departure from the standard scientific congress session, and underline the ERA-EDTA council’s wish to introduce more patient perspectives and patient-centred approaches into the Congress.

First-ever interactive role-play workshop

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How to Make Nephrology more ‘sexy’?

National Societies’ Meeting discusses ways to improve nephrology’s public image

On Thursday afternoon, the ERA-EDTA invited representatives of the national societies of nephrology to a joint meeting. The aim was to forge alliances, learn from each other and, thus, to strengthen European Nephrology. Representatives of 22 national societies attended the meeting. Professor Andrzej Więcek, President of the ERA-EDTA, first introduced the Association and presented its various activities and projects, from which national societies might benefit: The working groups, fellowship programs, the various publications, e.g. ndt and ckj, the European Nephrology Portal (ENP), and the Young Nephrologists’ Platform – just to mention a few. Professor Jonathon Fox, Secretary-Treasurer, then gave an overview of special projects that ERA-EDTA offers to national societies for participation: The National Village, the possibility to organize a CME with the endorsement of the ERA-EDTA, as well as the opportunity to submit short articles on national societies to the Newsletter ‘Follow us’. Doctor Ana Carine Ferreira, chairwomen of the Young Nephrologists’ Platform, outlined the platform’s activities, such as the YNP courses and the advisory program. This year’s congress president, Professor Jorge Cunhata, gave an update on the European Nephrology Exam, which can be taken in addition to national exams and will facilitate access to jobs in other European countries. This year, 77 doctors sat the exam, which was a great success taking into account that it has just been launched. Professor Raymond Vanholder, chairman of the European Kidney Health Alliance (EKHA), presented the results of a survey on patient choice of treatment – astonishingly, most patients are not informed about every option for renal replacement therapy (RRT), and if they are, the information is given shortly before dialysis is due.

However, the presentation that provoked most heated discussion was that of Professor Ziad Massy, Chairman of the ERA-EDTA Registry. He suggested ideas on how to improve fundraising in nephrology, and all participants agreed on his assumption that a pan-European marketing strategy is needed to raise awareness of kidney diseases. The tough task nephrologists have to tackle in the near future is to add some ‘sexiness’ to their specialty – because successful campaigning needs emotional appeal.
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