Current Perspectives in Kidney Diseases

Claudio Ronco^a Gaetano La Manna^b

^aDepartment of Nephrology, Dialysis and Transplantation, International Renal Research Institute of Vicenza (IRRIV), San Bortolo Hospital, Vicenza, and ^bDepartment of Experimental, Diagnostic and Specialty Medicine (DIMES) – Nephrology, Dialysis and Transplantation Unit, St. Orsola Hospital, University of Bologna, Bologna, Italy

The volume of *Contributions to Nephrology* entitled *Current Perspectives in Kidney Diseases*, edited by La Manna and Ronco [1], provides on the one hand an exhaustive presentation of the state of the art in different areas of nephrological research and on the other some helpful indications for daily clinical practice.

One of the mainstays of the volume is an emphasis on the kidney as the final ring of the complex chain of multiple organ failure. Recent advances in technology and research on the pathogenesis and therapies of sepsis-associated acute kidney injury (AKI), responsible for the high mortality incidence and progression toward chronic kidney disease (CKD), represent some important aspects discussed in the past and seem to be discussion topics for the present [2–9]. The last two decades have provided new insights into the pathophysiology of sepsis-associated AKI, correlating evident hemodynamic changes with the direct impact of several molecules on renal tissue. Improved knowledge of the pathogenesis of the disease has led to the discovery of some new potential therapeutic targets able to interfere with the mechanisms of tissue injury. However, large phase III clinical trials are still needed [10]. Sepsis-related AKI, or in general AKI, requires continuous renal replacement therapy. Achievement of the correct balance between any anticoagulation strategy

for the prevention of circuit blood clotting during continuous renal replacement therapy and the high bleeding risk related to AKI itself remains a critical issue in nephrological clinical practice. Ricci et al. [11] suggest the use of citrate as a successful alternative to common anti-coagulation strategies. As a result of the latest technological innovations, it can be used safely also in patients with a high risk of citrate accumulation, including during liver dysfunction [11].

In view of the key role of the kidney in multiorgan failure, descriptive and useful case series are reported, indicating novel possible applications of coupled plasma filtration adsorption for toxin removal during the course in liver failure or in serious medical emergencies, such as thyrotoxicosis [12].

The potential and clinical opportunities of new sorbent materials represent important topics of discussion in today's art of extracorporeal therapies. Discussions on new sorbents seem to shed light on some grey areas concerning the use of sorbents in acute and/or chronic renal replacement therapies [13].

In CKD, particular attention is paid to mineral metabolism, a well-known trigger of cardiovascular disease. Undeniably, the impact of phosphate represents a hot topic in current nephrology, as both hyper- and hypo-

phosphatemia are related to a shorter life expectancy in CKD patients. However, the optimal serum phosphate level to improve survival still needs to be identified [14]. In spite of the lack of dedicated randomized clinical trials, the review provides a comprehensive approach to phosphate balance, considering it a crucial but not a unique element of CKD-mineral bone disorder. This situation is further complicated by fibroblast growth factor 23 (FGF23), a hormone involved in mineral metabolism whose level rises during CKD, promoting urinary phosphate excretion. FGF23 has also been implicated in cardiovascular disease. The review by Grabner et al. [15] focuses on the most recent clinical and experimental data on FGF23 pathophysiology in CKD and its role as a cardiovascular risk factor.

Several questions regarding vascular access for end-stage renal disease patients undergoing renal replacement treatment have not been satisfactorily answered yet; in particular, when postsurgical stenosis of vascular fistulas occurs, palliative measures are almost always surgical due to the lack of effective drug treatments. New in vitro experiments suggest that CKD-related general vascular disease and the occurrence of fistula restenosis are strictly driven by the pathologic development of nondividing smooth muscle cells contributing to the growth of intimal atherosclerotic plaques [16].

A further spotlight has been placed on IgA nephropathy therapy, with an exhaustive overview on current KDIGO recommendations and on the still controversial use of mycophenolate mofetil as a therapeutic option for this disease [17]. The availability of “fast progression tests” in the most common hereditary kidney diseases such as autosomal dominant polycystic kidney disease is today a fascinating topic that requires research and studies [18].

It is also important to collect information on expert views on the future of hemodialysis. New developments of biomaterials and dialysis membranes able to optimize large solute removal with the highest possible albumin retention are of extreme interest today. New high retention onset membranes seem to allow application of a new technique and concept therapy named “expanded hemodialysis” [19]. Furthermore, to better understand potassium balance, a critical point to take into account in the course of hemodialysis, the section presents new mathematical models of solute kinetic and fluid shift during treatment to predict the real-time intracellular sodium and potassium concentration [20, 21]. The international trend for home dialysis programs as the first option for new patients completes the discussion on future perspectives in renal replacement therapies [22].

Renal transplant is still considered the treatment of choice for patients with end-stage renal disease [23], although management of the several posttransplant complications still represents an open question [24, 25].

Despite the advances in immunosuppression strategies, standard treatment for acute antibody-mediated rejection (ABR) is still being debated: in the last section different strategies for acute ABR, based on a strong immunological rationale, are introduced. Comai et al. [25] show that a plastic and pragmatic approach is needed. The authors review the literature and report a case series from a single-center experience; treatment strategies for ABR have to be evaluated case by case and they have to be led mostly by histological lesions. The use of antithymocyte globulin is suggested for ABR treatment, mostly in the case of concurrent T-cell rejection [25].

Given the huge immunological complexity of kidney transplants, one big challenge for the transplant community is represented by chronic allograft injury. The review by Madariaga and Riella [26] describes the latest prophylactic strategies for chronic allograft injury prevention based on new molecular findings, mostly gene expression analysis for patient risk stratification, or on more classical interventions on modifiable factors (hypertension, calcineurin inhibitor reduction, virus infection surveillance, and donor-specific antibody monitoring) [26].

Precision medicine is another important element in today's approach to kidney patients. The treatment management of transplant patients is generally initiated with protocols and then adjusted following serum drug levels or infection occurrence. Using a patient-tailored approach, recognition of the different individual immunological and genetic factors in kidney transplant recipients and donors might result in better outcomes for each patient. Recently, many assays have moved from the laboratory to the clinical arena, highlighting the promising option of individual treatment strategies and providing reproducible, noninvasive biomarkers with the potential to reduce allograft injury and quantify the alloimmune response [27].

The recent volume *Current Perspectives in Kidney Diseases* [1] represents therefore a guide for nephrologists who wish to be fruitfully updated on the ever expanding knowledge in our field but also for those who desire to increase their knowledge of parallel fields of medicine in a fully integrated multidisciplinary view. Several challenges remain open but it is important to know where to focus our attention and where to concentrate our efforts in research.

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