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Editorial Comment

EDITORIAL COMMENT

Deciphering the core elements around haemodialysis therapy

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ABSTRACT

The projected future demand for renal replacement therapies for patients with end-stage renal failure requires preparedness at different levels. The deliberations focus predominantly on the disproportionately high financial burden of care for patients on routine dialysis therapy compared with other chronic conditions. However, even today there are concerns regarding the shortage of healthcare workers in the field of nephrology. A substantial increase in trained healthcare professionals is needed for the future delivery and care of patients requiring haemodialysis (HD) that 89% of patients on dialysis receive; a sustainable health workforce is the cornerstone of any healthcare system. The multimorbid nature of chronic kidney disease as well as the complexity—especially the technical aspects—of HD are deterrents for pursuing nephrology as a career. An educational platform that critically examines the essential issues and components of HD therapy was thus considered appropriate to create or renew interest in nephrology. By providing broader and newer perspectives of some of the core principles around which HD evolves, with this set of articles we seek to facilitate a better appreciation of HD. We believe that such a reappraisal of either poorly understood or ill-defined principles, including usage of terminology that is imprecise, will help facilitate a better understanding of the functioning principles of HD.

Keywords: biocompatibility, evidence-based medicine, hemodialysis, membranes, sustainability

Such is the increase in chronic kidney disease (CKD) that by 2040 it is estimated to become the fifth leading cause of death globally; 10% of adults worldwide are now considered to be affected by some form of CKD [1]. Of the 10 most important drivers of increasing burden of diseases and injuries between 1990 and 2019, CKD is among the six causes that largely affects older adults [2].

With no cure for kidney failure patients in the near future, kidney replacement therapy is essential to sustain life [1]. Kidney transplantation is considered the best option, but wider utilization is restricted by the lack of sufficient donors. Thus dialysis remains the only viable alternative. Worldwide, 89% of patients on dialysis receive haemodialysis (HD), >90% of whom live in high- and upper middle-income countries[3]. A substantial number of kidney failure patients are still without access to maintenance dialysis. Only a fraction of the number of people needing dialysis actually receive it; millions are estimated to die prematurely because kidney replacement therapies could not be accessed [4–6]. Among the populations who have access to dialysis, mortality (mainly cardiovascular) remains high and outcomes are suboptimal despite the technological advancements, due to the high number of comorbid conditions associated with CKD as well as many other contributing factors [1, 3, 7]. Life expectancy of kidney

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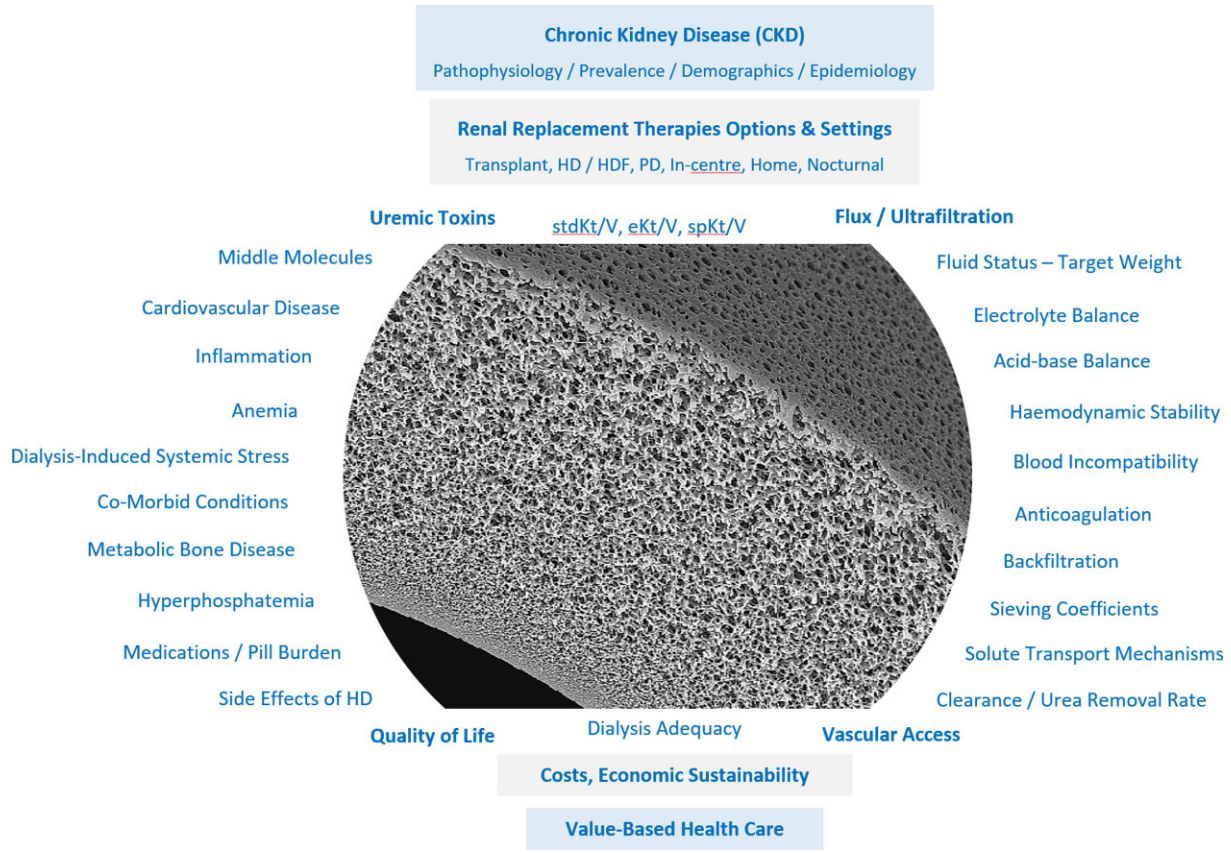

FIGURE 1: To cope with the projected future demand for kidney replacement therapies (especially HD), new nephrologists need to familiarize themselves with numerous medical, scientific and technological disciplines. In addition to the pathophysiology of CKD, clinical care of kidney failure patients requires consideration of multiple comorbid conditions and systemic biochemical pathways that afflict an increasingly aging patient population. The challenges are exacerbated by the need to understand complex scientific concepts and technological principles around which HD is based. With the worldwide difficulties in recruiting doctors and nurses for the care of dialysis patients, a concerted educational programme that is less daunting and aids better understanding of the complexities is required.

failure patients on HD may have improved over the years, but it is still on average only 5–10 years with a poor health-related quality of life [8, 9]. For a 20-year-old on dialysis, life expectancy is ∼40 years less than for the general population [10].

Faced with this sobering reality and despite implementation of strategies to prevent or slow the progression of CKD, coping with the expected global demand for HD therapy poses multiple challenges [11–13]. As an example, at the current rate of growth, the number of persons on kidney replacement therapy in Spain will hit 0.23–1.00 million by the end of the century, i.e. 1–4% of the projected population at that time [14]. While the (additional) economic burden is more readily assessable through model-based projections, there are complex issues—scientific, clinical and technical—that need to be better understood and addressed for the future preparedness of delivering dialysis therapies [15–17]. Although HD has evolved today into a safe procedure that is performed tens of millions of times each year, it is still largely constructed around empirical knowledge and concepts [18].

Beginning with the fundamental concept of clearance ('the *hypothetical* volume of blood from which a given solute is removed or cleared completely in a specific period of time'), the domain of HD is laden with numerous principles and definitions based on theoretical assumptions and formulae (Figure 1). Many formulations or conventions (e.g. middle molecules) have simply been carried on from the early experimental era in the 1960s–1980s without due deliberation of their present-day relevance [19, 20]. Some, like whether urea is just a marker (for clearance estimations) or a uraemic toxin or the *Kt/V* concept as a measure of dialysis adequacy, have been critically re-examined and are differently perceived today conforming to present-day learning [21–24]. Often the differences, interpretation and subtleties of the entities depicted in Figure 1 are only apparent to a minority who have delved into selected topics or to experts with extended experience and reputations in specialist subject matter. For the majority involved in nephrology, especially trainee residents, nurses or biomedical engineers considering specialising in HD, being able to discern between complex, multi faceted principles involving several scientific disciplines is simply too overwhelming. This complexity may also be one reason for the declining interest worldwide in nephrology as a career, raising workforce concerns and debates on the issue, despite the huge demand for skilled nephrology professionals now and into the future [25–27]. One reason is the disconnect between the sheer complexity—scientific and technical—of the HD procedure and the vast expansion of access to safe treatments in many healthcare delivery systems. Other reasons such as long working hours, having to deal predominantly with older patients with multimorbid conditions and comprehending the complex physiochemical principles and concepts (some of which are contentious) involved in HD are also deterrents to the selection of nephrology as a career.

It is with this primary concern—the need to attract and nurture a new generation of healthcare workers to help cope with the future demands for HD therapies—that the editors of *Clinical Kidney Journal* considered dedicating a supplement to address and revisit the defining elements of all HD therapies, with a special focus on dialysis membranes. The health workforce is the cornerstone of any healthcare system; an adequately trained nephrology workforce has been recognized as being critical to a sustainable kidney care system [25, 27, 28]. An educational platform that disseminates and critically examines the essence of key principles around which HD therapy evolves was thus considered appropriate to create or renew interest in the field of nephrology. The hollow fibre membranes of dialysers represent the 'central processing unit' of the entire blood purification function of dialysis. This supplement presents deeper insights into the world of membranes and their functions, including inadvertent interactions that occur during the procedure, to emphasize the two-sidedness of dialysis membranes.

Until around the 1960s, the prognosis of patients with kidney failure remained distressing and most uniformly fatal. Prior to that, a century of extraordinary endeavours had failed to provide a satisfactory solution to the dilemma of finding suitable semipermeable membranes that allowed the selective removal of uraemic retention solutes and excess fluid that accumulate in CKD. The advent of hollow fibre membranes affording large surface areas and fitted into more compact devices—dialysers—allowed the practical extracorporeal 'processing' of blood of patients and was a major landmark in nephrology. Just a decade or so later, in the mid-1970s, membrane and dialysis technology was sufficiently ripe to pave the way for routine treatment of kidney failure patients. Today, tens of millions of kilometres of hollow fibre dialysis membranes are produced annually using sophisticated technologies to cope with the increasing medical demands of chronic HD.

The four articles in section I of this supplement describe the commonality and peculiarities of natural and man-made membranes in relation to their ability to 'clear' blood of its 'toxic' content that builds up during uraemia. Insights into the principles involved in the making of hollow fibre membranes on a large scale emphasize not only the difficulties in emulating the functionality of their natural counterpart, but also the technological marvels and constraints involved to meet various clinical prerequisites. The fundamentals, as well as controversies and misconceptions (including nomenclature), surrounding uraemic toxicity and solute removal principles are thereafter discussed. Finally, the HD therapy modality choices and conditions under which the fundamental detoxification function can be achieved most efficiently in clinical settings are detailed against the backdrop of evidence-based and personalized medicine.

Section II of the supplement essentially deals with the 'other face' of membranes, transport processes or overall systemic effects of HD therapy as well as the economic constraints that increasingly compromise delivery of dialysis and impact clinical outcomes. Some of these issues are unavoidable consequences of extracorporeal circuits (ECCs) while others, if not adequately minimized or controlled, are detrimental to patient well-being in the short-term or negatively affect outcomes over longer periods. For the clinician, an understanding of the ramifications of adverse events occurring during HD needs to be balanced against the benefits HD therapy strives to achieve. Bioincompatibility, attributed mainly to the repeated contact of blood with artificial surfaces, will always be an issue to contend with in the absence of the protective effects of the endothelium in normal blood vessels. Blood–material interactions with different polymers of the ECCs occur even in the presence of anticoagulation. These reactions, together with induction of pro-inflammatory reactions occurring under certain circumstances by the transport or release (from polymers) of biologically active substances into the blood compartment, collectively contribute to the systemic stress condition that HD is now recognized to be. Clinical aspects of HD therapy that impede the attainment of satisfactory patient outcomes can no longer be dissociated from overall costs of care of HD patients. Coping with increased future demand for dialysis is intricately linked to implementation of more economically sustainable strategies [29, 30].

By providing broader and newer perspectives of the core principles around which HD therapies evolve, we sought with these set of articles to facilitate a better appreciation of HD. We believe that the reappraisal of either poorly understood or ill-defined principles, including usage of terminology that is imprecise, will help facilitate a better understanding of the functioning principles of HD. Above all, we hope the educational value of this treatise renews or creates interest in the field of nephrology.

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CONFLICT OF INTEREST STATEMENT

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