Recent decades have witnessed remarkable changes in the treatment of ESRD, particularly in the large-scale provision of maintenance dialysis. Initially, nephrology’s main dialysis-related challenge, corresponding roughly to the period from the 1960s to the 1980s, was to transform dialysis from an obscure therapy delivered in comparatively few locations into a readily accessible, sustainable treatment regimen capable of being widely delivered. The period from the 1990s to the present has been characterized by further developments of dialysis as an enterprise, including the need to meet the explosive growth of ESRD in developed countries (most notably in the United States), the technologic advancements in dialysis membranes and machines, the introduction of erythropoietin alfa, and the maturation of research tools, such as the US Renal Data System, to study a public health phenomenon that has grown larger than most anyone would have predicted.

Is dialysis now entering yet a new era? A strong case could be made that the daunting challenges facing the health care community and government health ministries worldwide are now coming into sharp relief. There is evidence that this new era will be characterized by falling death rates—and resultant lifespan increases—of patients on “prevalent” dialysis in industrialized countries coupled with profound growth in the incident dialysis population in developing regions of the world, particularly South America, sub-Saharan Africa, India, China, and throughout the rest of Asia.

Recent work has highlighted the immensity of the challenges that must be faced. In this issue of JASN, Thomas et al. render several insights of major importance for policy planners, government officials, researchers, physicians, and other providers who care for patients receiving dialysis. Thomas et al. estimate that there has been approximately 70% growth in prevalent patients between 1990 and 2010 and report that the number of patients who are treated with maintenance dialysis reached approximately 284 per 1 million population in 2010; for a current worldwide population of approximately 7.2 billion, this represents roughly 2 million patients. This finding is broadly consistent with another recent estimate of a total of 2.6 million as of 2010. During the same period, global incidence more than doubled from 44 to 93 per 1 million population, a worldwide incidence of nearly 700,000 new patients per year.

What might account for these developments? According to Thomas et al., changes in population structure driven primarily by population growth and aging seem to account for only approximately 25%–35% of the increase in patients on prevalent dialysis. The increases in diabetes and hypertension, the two most common causes of ESRD, in the general population also seem to play a substantial role. However, Thomas et al. suggest that the single largest contributor to the growth of the dialysis population is governmental support for maintenance dialysis programs. If true, this suggests that governments are attempting to respond to the growing need for maintenance dialysis in their populations—a very welcome development indeed. However, somewhat more ominously, these results suggest that there is a vast unmet need for dialysis and that if dialysis could be universally provided on a global scale, the number of patients receiving maintenance dialysis might increase abruptly. Indeed, a recent study reports that, using a conservative analytic approach, perhaps 2.3 million individuals requiring RRT died prematurely, because they could not access it; a more liberal approach put the total at a truly daunting estimate of 7.1 million premature deaths. This “RRT gap” can, therefore, be conceived of as the true present need for maintenance dialysis or kidney transplantation, even before considering future growth of the population (expected to reach 9.6 billion in 2050), the aging of the population, or the increases in rates of diabetes and hypertension that are occurring as the world’s population urbanizes and becomes more affluent.

An important distinction must be made between countries that provide universal dialysis access and those that do not, a distinction without which the understanding of dialysis growth is incomplete. In the countries where universal access is provided, such as the United States and the countries of western Europe, incidence rates have recently stabilized, and growth in the overall dialysis population has been driven by patients on prevalent dialysis who are now, on average, living longer. For example, there have been approximately 110,000 incident dialysis patients annually between 2006 and 2012.
However, the mean lifespan has increased approximately 20% from 5.5 years in 2003 to 6.6 years in 2012. Whether stabilization in the incidence counts will continue in the most affluent nations is unclear but seems unlikely: data from the World Health Organization show falling rates of death caused by cardiovascular disease in the general population, rates that are now exceeded by cancer death rates (which are themselves decreasing overall) in many affluent countries. This may mean that individuals with CKD who formerly died from cardiovascular complications will now live to require RRT. This phenomenon might be compounded by ESRD caused by chemotherapy or other cancer-related etiologies, because falling rates of cardiovascular death may mean that more patients will live long enough to develop cancer. As a result, incident ESRD counts in the United States alone may increase to >140,000 per year by 2020, at which time the prevalent United States ESRD population may exceed 700,000.

In countries that provide partial dialysis access, the RRT gap is immense. In Asia alone, 1.9 million people may need RRT but do not receive it according to a conservative estimate; even with a large persistent gap, the number of patients who do receive dialysis seems likely to double from 1.0 to 2.0 million between 2010 and 2030. Because the factors driving the growth of ESRD are not fully understood, it is possible that the rapid economic growth characterizing India, China, and other Asian nations may mean that projections of ESRD growth are underestimates.

How might the world rise to meet these challenges? Prevention is critically important. Global efforts to control diabetes, hypertension, and perhaps, hyperlipidemia seem an appropriate place to start. Screening for CKD is somewhat more controversial; although some entities have in the past suggested a role for universal screening, targeting at-risk individuals, especially those with diabetes and hypertension, may be more cost-effective. Asia is a special case regarding screening: IgA nephropathy, a common cause of ESRD in this region, might be missed by a strategy focusing on diabetes and hypertension. However, it is likely that many more individuals will live with CKD caused by IgA than will progress to ESRD because of it, and so whether it is appropriate to geographically tailor screening is unclear. Likewise, the transition to ESRD must be managed more effectively. For example, efforts to identify potential living related kidney donors must intensify in an attempt to provide preemptive transplantation. The appropriate use of conservative care (that is, management that does not involve dialysis initiation) must be soberly debated in every country, ideally in an environment in which foregoing dialysis is a result of free choice rather than a reflection of a society’s inability to provide universal RRT.

Additionally, the economics and the physical mechanics of how to meet the world’s growing dialysis needs must be confronted. Provision of traditional three times per week hemodialysis, long the most common form of RRT in most developed countries, would require immense infrastructure investment and, particularly in countries with large impoverished rural populations, logistic challenges. Whether the “bricks and mortar” investment characterizing in-center hemodialysis can ever be met by nations struggling with competing health care priorities is dubious. Other RRT modalities, such as peritoneal dialysis or home hemodialysis, may help meet this need, but these therapies entail their own challenges; peritoneal dialysis requires a logistic infrastructure where dialysate can be reliably delivered, and home hemodialysis requires abundant access to water. Additionally, in-center hemodialysis may well be necessary as a backup should these modalities fail.

Finally, the world requires better mechanisms for CKD and ESRD surveillance. National registries in developing countries in particular are an urgent priority, so that changes in disease patterns can be studied and researchers can leverage the natural experiments that occur during the course of rendering care, the niche for which observational research is so uniquely well suited.

In the past half century or so, dialysis has burgeoned into the first true organ replacement therapy accessible to millions of people. For this, the nephrology community can be justifiably proud. However, a new era may well be upon us as the population grows, ages, becomes more affluent, and finds itself less likely to die early from cardiovascular-related deaths. Thomas et al. show how this growth has unfolded since 1990 and provide insights as to how it might continue to unfold. Whether and how governments and their health care systems can close the present RRT gap while keeping abreast of future ESRD growth will be the great dialysis challenge of the next half century.

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DISCLOSURES

None.

REFERENCES


A Transcriptional Map of the Renal Tubule: Linking Structure to Function

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Differentiated organ function is critically dependent on the coordinated expression of a specific set of genes. Nephron segment-specific genes define the key functional characteristics of the kidney. Manual microdissection of the kidney into distinct tubular segments has provided unique insights into the function and failure of the kidney.1

The initial studies into the electrophysiology and biochemistry of microdissected tubular segments have subsequently been expanded using the tools of molecular biology to capture the molecular components defining the tubular microenvironments. Early studies focused on the gene expression of specific molecules of interest and were greatly facilitated by the development of ultrasensitive reverse transcription polymerase chain reaction.2 As transcriptional profiling techniques matured, more genome-wide approaches could be deployed on microdissected tissue. The landmark study from Chabardès-Garonne et al. used serial analysis of gene expression (SAGE) to define transcript maps from the main nephron subunits.3 Subsequent studies used predominantly Affymetrix-based hybridization platforms to generate expression profiling of glomeruli and tubular segments from animal models and human tissues in health and disease. These studies allowed transcripts to be catalogued to the main nephron units to be catalogued, but still had limits to the sensitivity and spectrum of transcripts detected. The introduction of next-generation sequencing technologies to transcriptional profiling of RNA (RNA-seq) now allows the transcriptome to be captured with unprecedented depth and sensitivity. In addition, RNA-seq can detect the complexity of alternative spliced transcripts in a sample. This is of particular relevance for tissue compartment-specific regulation, as the majority of multiexon genes in humans undergo alternative splicing to increase the functional diversity of protein species4 and are not comprehensively detected by most microarray platforms.5

In this issue of the *Journal of the American Society of Nephrology*, Mark Knepper and his team report the most

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