Published in final edited form as:

Semin Nephrol. 2009 November ; 29(6): 549–550. doi:10.1016/j.semnephrol.2009.07.014.

Aging and the Kidney: Introduction

Gary E. Striker, MD,

Mount Sinai School of Medicine, New York, NY

Helen Vlassara, MD, and

Mount Sinai School of Medicine, New York, NY

Luigi Ferrucci, MD

National Institutes of Health, Baltimore, MD

This issue of *Seminars in Nephrology* addresses a controversial and important topic that presents at least two sobering challenges to the nephrology and geriatrics communities. Namely, the widely held view that renal function decreases with age may need to be reevaluated because new data suggest that not all aging persons are affected. If these data are confirmed it is critical to understand the reasons underlying the presence or absence of declining renal function. Second, of the many kidney functions that might be affected, it is not clear which one (or a combination thereof) represents the most significant risk for damage to other organs in the individual aged person. However, if the changes do not reach a critical functional threshold, they may not have a negative impact on health span, and are simply an unimportant laboratory value. They do not represent a disease and the nephrologist, geriatrician, and general physician populations can advise their patients of this fact. Nonetheless, it is important to reconsider causes and consequences of changes in renal function with aging because it is becoming quite clear that this process has negative consequences on multiple organ systems and because new treatment options may be available. For instance, high blood pressure, a common problem in elderly patients, is a modifiable risk factor for cardiovascular diseases and is associated with increased risk of heart attack, heart failure, stroke, and kidney failure. In fact, Burney and Bakris stated that 67% of US adults aged 60 and older are hypertensive. A clear interpretation of this statistic is complicated by the fact that women and men aged 70 and older are significantly less likely to control their hypertension than those aged 60 to 69. Baylis found that women develop less age-dependent loss of renal function than men, in part because of cardiorenal protective effects of estrogens. The causes of changes in renal function include a deficiency of nitric oxide, and preservation of nitric oxide production in females contributes to better cardiovascular and renal responses in aging.

Focusing on renal function decline becomes more and more important as we start understanding its increasing prevalence with aging and its impact on the global health and physical function in older individuals. As the number of older individuals increases in the US population, the economic and health care burden caused by age-related chronic diseases, such as declining renal function, also increases. Eggers noted that although the rate of growth of the end-stage renal disease (ESRD) population may be slowing, the increasing number of aging persons who appear to have reduced renal function, without other evidence of primary renal disease, remains as a thorny issue because it generally is agreed that

reduced renal function carries an increased risk of aging-related diseases. Muntner states that there is a paucity of data on longitudinal changes in glomerular filtration rate in aging and points to the need for more studies in the aged. One problem for those who study renal function in aged individuals without clinically evident chronic kidney disease is the question of how to reliably measure renal function, what renal function to measure, and how to tell random variability from true changes. These questions have complicated our ability to verify or refute the paradigm that renal function declines with age among adults, and emphasizes the need to develop better measures of renal function to assess longitudinal changes and their association with aging-related diseases in other organs. This is particularly important because 35% of individuals without renal disease followed up for up to 23 years in the Baltimore Longitudinal Study of Aging did not experience a decline in renal function, despite the fact that analysis of the overall cohort showed that creatinine clearance declined by a mean of $-0.75 \text{ mL/min/1.73 m}^2$ per year. These data emphasize the variability in the number of persons who experience a decline in renal function with age, and the importance of determining whether a laboratory value indicating a decline in renal function, such as a decreased estimated glomerular filtration rate, has pathophysiologic significance. This dilemma is addressed in the aging population in the article by Himmelfarb, who reports that a steady increase in the incidence of acute kidney injury and development of ESRD is associated strongly with advancing age in the population. This may be owing to heightened susceptibility to drug toxicity, and/or the fact that the elderly consume twice as many medications as younger patients. This is complicated further by renal tubular defects detailed by Sands et al, who found that aged people and rats have a reduced ability to maximally concentrate their urine, possibly because of a reduction of key transport proteins that contribute to urine concentrating in the medulla of aged rats. The end result is that elderly subjects with acute kidney injury are more likely to develop ESRD. Other changes in aging include increased gene expression in individual glomerular cell types that Wiggin et al and others have found to be influenced by diet and genetics. Finally, in this area, Zheng found that inflammatory changes are present in both renal parenchymal cells and inflammatory cells in aging, especially when the levels of oxidants (ie, advance glycation end products [AGEs]) are increased. Because AGEs cause cell injury, these data may explain the decreased ability of the aged kidneys to excrete AGEs, which results in overall increases in inflammation and oxidant stress in the body.

On a more practical note, Huang et al found that there is an increasing rate of transplantation in the elderly, even though the patient survival rate is lower in aging recipients. Choudhury et al found that the older population with chronic kidney disease is at greater risk for cardiovascular disease, and reduced renal function represents an independent risk factor. Although changes in lipid metabolism, which have significant atherogenic potential, suggest that statins may be of benefit in cardiovascular outcomes and progression of kidney disease in younger patients, randomized trials have not been performed to determine if there are similar benefits and targets of treatment for dyslipidemia in the elderly. With respect to ESRD in the elderly Sherrard provides many practical hints to control various aspects of bone disease and fracture, although he notes that clinical trials are sorely needed and should be conducted. In the same vein, Dunkovic found that although elderly persons are a

heterogeneous population, dialysis provides a good quality of life and survival for many patients with end-stage kidney disease.

This issue of *Seminars in Nephrology* emphasizes the challenges and opportunities that remain in understanding the response of the kidney to aging, the potential approaches to modulation of changes, and addresses a topic of renewed interest to those interested in basic and clinical research, as well as the care of the aging adult.