

## Robert W Schrier, an influential observer from outside Hepatology (1936–2021)

Robert William Schrier, one of the greatest nephrologists of all time, died on January 23, 2021. He is survived by his beloved wife Barbara, his five children and a number of grandchildren. It is not common that a top specialty journal publishes an obituary about a physician from another specialty, unless he/she has made exceptional contributions to the field. This is the case of Robert W Schrier whose vision from the Nephrology field provided important clues to unveil some very relevant pathophysiological “mysteries” of Hepatology, on the formation of ascites and edema and the development of kidney abnormalities in liver diseases.

As a nephrologist, Robert W Schrier became fascinated by the fact that the kidneys of patients with cirrhosis developed major functional abnormalities without an underlying structural cause. He devoted an important part of his career to this field by answering very relevant questions: i) why patients with advanced cirrhosis develop such an important alteration of sodium homeostasis so that they are almost unable to eliminate sodium in the urine?; ii) why the subsequent expansion of plasma volume caused by sodium and corresponding water reabsorption is unable to turn off the signal(s) to the kidneys so that patients have persistent sodium retention, despite a remarkable increase in body sodium and the existence of ascites and edema?; and iii) why the kidney disturbance in some patients becomes so important that they develop very severe functional renal failure without structural abnormalities, the so-called hepatorenal syndrome (HRS)? To answer these questions, Robert Schrier developed the hypothesis that in major edematous states, such as cardiac failure or cirrhosis, patients develop sodium retention due to decreased “effective arterial blood volume” which is the cause of the afferent signal to the kidneys that triggers sodium retention.<sup>1,2</sup> Sodium retention in renal tubular cells is mediated by some important neurohumoral factors activated in response to the reduction in effective arterial blood volume, such as the renin-angiotensin-aldosterone system, sympathetic nervous system, and antidiuretic hormone, arginine-vasopressin.<sup>3,4</sup> In simple terms, the afferent signals to the kidney derive from an underfilling of the arterial circulation. In the case of cirrhosis, this underfilling is due to a marked vasodilation of the splanchnic arterial circulation probably related to an increase of vasodilator mediators, particularly nitric oxide (NO), due to cirrhosis-related portal hypertension.<sup>5–7</sup> This is the basis of one of the most famous theories in Hepatology: “The arterial vasodilation theory of ascites and edema formation in cirrhosis” that was proposed in 1988 and has since stood the test of time.<sup>8</sup> New data suggests the potential relevance of systemic inflammation in the pathogenesis of kidney dysfunction in cirrhosis, but its role has not been demonstrated convincingly as yet.<sup>9</sup> By contrast, the arterial vasodilation theory and a number of studies developed by Robert Schrier’s group constituted the pathogenic basis for the management of HRS with



vasoconstrictors, particularly terlipressin, which currently represents the standard of treatment for HRS according to international guidelines.<sup>10–12</sup>

Besides his contributions to Hepatology, Robert Schrier made very relevant contributions to Nephrology, particularly in the field of hyponatremia, mechanisms of acute tubular injury, polycystic kidney disease, and diabetic nephropathy, among others. He was president of the most important national and international societies of Nephrology and founding editor of *Nature Reviews Nephrology*. He also edited a large number of books, particularly the major textbook “Schrier’s Diseases of the Kidney” that has served and is still serving generations of nephrologists and internists worldwide.

Robert Schrier spent most of his career at the University of Colorado in Denver where he was Chief of the Division of Renal Diseases for 20 years. This division achieved an extremely high reputation for clinical assistance and research. Several hundreds of physicians and investigators from around the world joined the Division over the years as faculty, house staff, visiting professors or fellows. He also served as chairman of the Department of Medicine at the University of Colorado for 26 years (1976 to 2002) and created one of the most successful and respected Departments of Medicine throughout the United States by recruiting very talented Division Heads, increasing research funding, and focusing on the training of house staff and students.

For those who knew him, his main legacy has to be the passion he had for life, his family, sports, especially basketball, cultural diversity as well as medicine. He was driven and determined to make things happen, he had enormous capacity

for work, and he built enduring friendships around the world. These are the main gifts to those who worked with him. Nephrology has lost one of its big names, but Hepatology has lost one of its most influential observers.



<https://hoopshall.com/inductees/?inducted-year=2004> Image of Robert W Schrier posted in the Indiana hall of fame of basketball. He played for DePauw University team and still holds one of the highest 4-year scoring averages.

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Pere Ginès\*

*Liver Unit, Hospital Clínic of Barcelona, Faculty of Medicine and Health Sciences, University of Barcelona, Barcelona, Spain*

\*Corresponding author. Address: Liver Unit, Hospital Clínic of Barcelona, Faculty of Medicine and Health Sciences, University of Barcelona, Barcelona, Spain.

*E-mail address: [pgines@clinic.cat](mailto:pgines@clinic.cat)*

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