

## New Studies in the Pipeline with Endothelin Inhibitors

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Glomerulosclerosis [FSGS]: A Randomized, Double-blind, Active-Control, Dose-Escalation Study) (9), a phase 2 trial, studied the effect of 200 mg, 400 mg, and 800 mg daily in primary FSGS. All doses of sparsentan compared with 300 mg of irbesartan achieved greater reductions in the protein-to-creatinine ratio (45% vs. 19% with 200 mg; 47% vs. 19% with 400 mg and 800 mg). Blood pressure was also reduced in the sparsentan group, and estimated glomerular filtration rate (eGFR) was stable in both treatments. The incidence of adverse events was similar between groups. Moreover, a post hoc analysis (DUET-Open-Label Extension [OLE]) concluded that 40% of patients treated with sparsentan achieved complete remission of proteinuria ( $\leq 0.3$  g/g) on at least one occasion (10).

DUPLEX (Study of Sparsentan in Patients with Primary FSGS) (11) is the phase 3 study that will evaluate the long-term antiproteinuric efficacy, nephroprotective potential, and safety profile of sparsentan compared with irbesartan in patients with primary FSGS. Also, in immunoglobulin A (IgA) nephropathy, which is the most prevalent primary glomerulonephritis worldwide, the potential benefit of 200–400 mg of sparsentan on kidney function will be evaluated by analyzing changes in proteinuria and eGFR as compared to 150–300 mg of irbesartan in the PROTECT study (A Study of the Effect and Safety of Sparsentan in the Treatment of Patients with IgA Nephropathy; ClinicalTrials.gov: NCT03762850).

Sodium glucose co-transporter 2 inhibitors (SGLT2i) cause, through tubuloglomerular feedback, afferent arteriole vasoconstriction and have also proven kidney protection from CKD progression (12). Therefore, a potent antagonist of ETA with no effect on the ETB receptor (zibotentan) is being evaluated in ZENITH-CKD (Zibotentan and Dapagliflozin for the Treatment of CKD), a phase 2b study in patients with CKD and proteinuria (ClinicalTrials.gov: NCT04724837), as monotherapy and in addition to the SGLT2i, dapagliflozin. Zibotentan has already been studied

in ZEBRA (Zibotentan Better Renal Scleroderma Outcome Study; ClinicalTrials.gov: NCT02047708), with positive results in the scleroderma renal crisis.

In conclusion, ERAs are a strategic therapy with promising effects on proteinuria and CKD progression. However, their incorporation into clinical practice has been delayed as a consequence of their adverse effects in terms of fluid retention. New molecules seem to achieve results with statistical power and safe results that will finally allow us to include them soon in day-to-day practice. In the near future, the treatment of patients with CKD is expected to mimic the sequential treatment offered currently for patients with heart failure. ■

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## How We Learn Principles and Perspectives in Nephrology

By Tiffany Truong, Matthew R. Sinclair, and Sam Kant

Medical education, like medicine itself, has evolved over time—from the days of professional guilds and apprenticeships to the establishment of structured postgraduate residency training to duty-hours' restrictions, changes in licensing exams, and the growth of innovative educational resources (1). As the design of medical training changes, so too does the type of physician it produces. After all, medical education is not simply the acquisition of knowledge or even of skills and experiences but a process of shaping and the metamorphosis of the learner.

In a field like medicine, interwoven as it is with the science and humanity of life, the training is not only transformative but also inherently lifelong. Learning—and teaching—becomes a skill in itself. *How we learn* in addition to *what we learn* is pivotal to the type of physician we become. How then do we learn best? If we are to shape our own transforma-

tion in the years of our formal training in nephrology, what constitutes a “good” education? And what currently is the landscape of this training in nephrology?

To answer these questions, we gathered a few perspectives from a group of nephrology fellows and attendings with backgrounds in medical education and surveyed the literature on frameworks of adult learning as it may apply to medical training.

In the 1960s, Malcolm Knowles described an early theory of adult education that he called “andragogy” (in contrast to “pedagogy” for education during childhood, although this is acknowledged to be a continuum) (2). The basic principles of andragogy are assumptions about how adults learn. Among these assumptions are that adults must want to learn, that they need to know the reason for learning something and its relevance, that they are more centered on problem solving and their experiences, and that they need to be self-motivated or responsible for the planning of their instruction (2).

What we heard from both nephrology fellows and attendings was strikingly consistent with these assertions. Foremost, a sense of purpose and relevance is important. Many reported that learning is most effective when the applicability is clear, citing a preference for teaching that focuses on clinical relevance, for example, with bedside teaching and case-based approaches. Clinical experiences and the application of physiologic principles in a clinical context are the core of medical training, and learning this explicitly provides direct applicability. In particular, Free Open Access Medical Education (FOAMed) has been cited as a valuable resource to meet the challenges to early engagement in nephrology, including

the perception that it is very technical, making it difficult to appreciate clinical applications early on (3).

Yet, clinical context is not enough. We cannot encounter every clinical scenario either directly or through cases. In another model of education—Kolb's cycle of experiential learning—learning is a cycle of feeling (having experiences), watching (observing and reflecting), thinking (abstraction and generalization), and then doing (applying concepts in new situations) (2). Learners have different strengths in this cycle, for example, “activists” who feel and do, “theorists” who watch and think, or “pragmatists” who think and do (2). In medicine, “feeling” would equate to having a clinical experience, and “doing” would mean applying that experience to a new situation. The concrete steps of having an experience and being able to apply that experience are separated by the more abstract steps of reflection and abstraction, which also allow for generalization. For many fellows, effective learning is not only about gaining clinical experiences but also involves how best to reflect and process information outside of the clinical environment.

In this regard, educational resources in nephrology abound with options to engage learners of every kind, with many recommendations for textbooks, auditory or visual material such as podcasts and pathology videos, question sets, as well as virtual courses and simulations of clinical cases. Leticia Rolon, MD, a nephrology attending and educator at the University of California in San Francisco, states, “Different platforms have different strengths. For acid-base and electrolyte physiology, you can go back to basics and read Burton Rose. But you don't have to read it alone now—you

can listen to a podcast called *Channel Your Enthusiasm* to add some comedic relief or clinical pearls. The National Kidney Foundation's (NKF's) *Primer on Kidney Diseases* is good for learning glomerulonephritis. And for fellows studying for the boards, I enjoyed the ASN Board Review Course."

Both nephrology fellows and attendings have championed FOAMed as "an interactive learning experience," which can be "more digestible" and simply "fun." Regardless of the media, the key is, as Dr. Rolon states: "A good medical education in general focuses on foundational concepts that are applicable broadly. Be an expert in what you do, and know the basics of everything else. This is the idea behind novel teaching programs [that] focus on diagnostic schemas and pattern recognition. The focus is not on memorizing details disconnected from each other, but on building upon levels of understanding and tiered learning."

Beyond the resources granted to us by the teachings of well-known but faraway nephrologists, professional societies, and social media, resources that are closer to home and institution specific can also be invaluable. Helen Johnson-Wall, MD, a second-year nephrology fellow at the Medical College of Georgia, advocates for interactive approaches, including chalk talks by faculty and flipped classroom approaches where small group discussions are held after individual reading at home. Other nephrology fellows tout dedicated time with a nephropathologist and institution-specific resources. Raad Chowdhury, MD, the chief nephrology fellow at the University of Pittsburgh, remarks, "One of the resources I am very proud of at our institution is the University of Pittsburgh's Renal Handbook, titled *How to Avoid Spilling the Beans*. It is essentially a survival guide created by esteemed faculty to help fellows stay afloat.... It is practical, clear, and concise."

Another interesting aspect of self-motivation and the desire to guide our own instruction is the value fellows place on engaging in teaching themselves. The common adage in medical training states we must "See one, do one, teach one." Most nephrology fellows reported enjoying teaching, and some reported it was useful to their own learning. However, this enthusiasm was not uncommonly tempered by limitations in time due to competing interests, including their own need for dedicated time to learn. Indeed, time is frequently our most precious resource. Dr. Rolon asserts that although the responsibility of the educator is to highlight important teaching points and their relevance, and the responsibility of the learner is to bring forth intellectual curiosity, the learning environment itself must provide clinical experiences while allowing trainees the time and space apart from their responsibilities to build on their curiosity and avoid burnout.

What makes an excellent nephrology fellowship? Dr. Rolon and Matthew Sparks, MD, the program director of the nephrology fellowship program at Duke University, both find that the key to a successful program is its ability to adapt to the complex and evolving nature of nephrology as well as the diverse interests, strengths, and aspirations of its trainees. Dr. Sparks states, "The program should excel in allowing fellows to achieve excellence in patient care, have a longitudinal comprehensive curriculum, provide growth and development opportunities, and most importantly, give the same level of attention to each fellow regardless of career path."

As we embark on a new year and reflect on the past, many nephrology fellows are sum-

miting the halfway point of the academic year. Faculty have started to anticipate newly matched incoming classes. We recognize the breadth and depth of lessons left to teach and learn and remain ever thankful for these seasons of change that bring opportunities for new growth and fresh beginnings. ■

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## 2021 AASLD Guidance update confirms...



# THE KIDNEYS CAN'T WAIT SOONER IS BETTER FOR HRS-AKI / HRS-1<sup>1,2</sup>

The American Association for the Study of Liver Diseases (AASLD) has updated their Guidance with a key recommendation: elimination of an absolute serum creatinine (SCr) threshold for diagnosis of hepatorenal syndrome acute kidney injury (HRS-AKI / HRS-1). This Guidance, which aligns with a 2015 recommendation from the International Club of Ascites (ICA), may lead to earlier diagnosis and improved treatment outcomes.<sup>1,2</sup>

- Earlier treatment by approximately 4 days<sup>3</sup>
- Initiation of treatment when SCr levels were, on average, approximately 1 mg/dL lower<sup>3</sup>
- Treatment before a further  $\geq 1.5$ -fold increase in SCr (in 47% of patients)<sup>3</sup>

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