POINT-COUNTERPOINT

INTRODUCTION TO POINT-COUNTERPOINT: MECHANISMS OF GLOMERULAR FILTRATION: PORES VERSUS AN ELECTRICAL FIELD

There are clear physiological differences between glomerular and peritoneal capillaries. For example, charge and size selectivity play a greater role in filtration at the glomerular than the peritoneal capillary (1), whereas the peritoneal capillary is much more permeable to large molecular weight proteins such as albumin, behaving more like the nephrotic than the normal glomerulus. Anatomical comparisons are limited since there is no analogy to the glomerular slit membrane in the peritoneal capillary. Similarities exist, however, and the traditional pore model has been used to describe the movement of solute across both capillary sites. A recent hypothesis challenges glomerular pore theory, suggesting that electrical fields may play a more fundamental role in explaining glomerular permeability to proteins than that which has been previously considered based on traditional Ficoll filtration studies. This forms the basis of our debate—first presented at the EuroPD meeting in Maastricht in 2013.

Moeller and Kuppe (this issue of *PDI*), from the University of Aachen, propose electrical field theory. The “electrokinetic model” is based on the concept of a barrier generated by a streaming potential acting as a dynamic electrical field across the glomerular filtration barrier, proportional to the filtration pressure across the membrane, distinct from charge selectivity, and preventing negatively charged plasma proteins from entering or passing the filter. Their hypothesis is based on work conducted in *Necturus maculosus* (the common mudpuppy—a species of salamander) since the mammalian glomerular capillary cannot be micropunctured due to its small size (2). They present several arguments against pore theory, such as the absence of pores seen by electron microscopy on the mammalian glomerulus; difficulties with the mathematical model that is currently used to describe the filtration of albumin across the glomerular membrane; and the question of how “clogging” would be avoided in the pore model.

Of course the characteristics of glomerular filtration are difficult to measure and require the use of tracer probes combined with mathematical modeling (3). The 2-pore model of capillary permeability has been utilized to describe the transport of water and plasma solutes in a large number of organ systems and its application to glomerular filtration is defended by Rippe and Öberg from Lund University (this issue of *PDI*), who discuss the charge-selective filtration barrier, reviewing the evidence

for this traditional model based on the sieving of Ficoll (4). They challenge the significance of the electrophoretic forces described by the Aachen team, suggesting that the electrokinetic contribution to albumin transport has been overestimated and that the polarity of the streaming potential has been reversed, possibly relating to structural differences between the *Nectarius* and the mammalian glomerular basement membrane?

What can non-physiologists learn from this exchange of ideas? This debate provides an insight into the exploration of physiological processes that underpin our basic comprehension of nephrology. It reminds us that our understanding of such principles is based on detailed experimentation and subject to the impact of variations in method, species, and interpretation. In addition, it is instructive to consider the differences between glomerular and peritoneal capillary function. Finally, it reminds us of the importance of being prepared to re-evaluate paradigms that we hold as true in order to advance the understanding of our specialty.

DISCLOSURES

The author has no financial conflicts of interest to declare.

Martin Wilkie

Sheffield Kidney Institute
Sheffield Teaching Hospitals NHS
Sheffield, South Yorkshire, UK

email: Martin.Wilkie@sth.nhs.uk

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