Correspondence

To the Editor:

I enjoyed reading the article "New insights into the pathoanatomy of diabetic macular edema: angiographic patterns and optical coherence tomography" by Byeon et al.[1] The authors are to be commended for their detailed discussion of the regional blood supply and the neural architecture of the macula along with their optical coherence tomography correlations.

The authors point out that both layers of the deep retinal capillary plexus are confined to the retina's inner nuclear layer. Because fluid leaking from a retinal capillary would initially accumulate around that leaky capillary, one would expect that diabetic macular edema would predominantly affect the retina's inner nuclear layer. Another reason to expect that macular edema would be confined to the inner nuclear layer is because, as the authors point out, "The synaptic junctions within the outer plexiform layer and the inner plexiform layer have been known to act as a highly resistant fluid barrier."[2] Therefore, the inner and outer plexiform layers (OPLs), which sandwich the leaky capillaries in the inner nuclear layer, would be expected to confine the bulk of the intraretinal fluid to the inner nuclear layer. Yet, as is beautifully illustrated in the article, diabetic macular edema predominantly affects the outer nuclear layer (ONL) and only minimally affects the inner nuclear layer.[1]

The explanation offered in the article for the puzzling location of diabetic macular edema in the ONL is "A large number of microaneurysms directly encroached onto, disrupting the integrity of the synaptic portion of the OPL, or at least lied adjacent to it. In this situation, fluid from the leaking source can move into adjacent tissues with less resistance."[3]

I am writing to suggest other possible mechanisms by which fluid could accumulate in the ONL of the retina when the source of the fluid is the leaky capillaries in the inner nuclear layer. First, in the diseased diabetic retina, the integrity of the OPL could be compromised by ischemia. This disruption of the OPL could decrease its function as a highly resistant barrier to fluid flow. If the OPLs were not resistant to fluid flow, fluid from the inner nuclear layer could pass through it and accumulate in the ONL, which is avascular. Second, over time, even a relatively small amount of fluid would be expected to trickle through an intact OPL, despite it being a highly resistant barrier. That trickle of fluid would become trapped between the OPL and the external limiting membrane and slowly accumulate over time because this regions is avascular and therefore lacks an efficient fluid removal system. Finally, there may be an active transport mechanism involved that shuttles proteins into the ONL. Because the ONL is avascular, it relies on surrounding tissue for nutrients. Such an active transport mechanism might concentrate proteins in the ONL increasing the oncotic pressure and subsequently attracting fluid resulting in retinal edema.

Because there is no experimental evidence at the moment to support one hypothesis explaining the accumulation of fluid in the ONL in the retina of patients with diabetic macular edema, I think it worthwhile considering these alternative possibilities not mentioned in the article.

Steven Cohen, MD
Retina-Vitreous Associates of Florida
Clearwater, Florida

References

1. Byeon SH, Chu YK, Hong YT, et al. New insights into the pathoanatomy of diabetic macular edema: angiographic patterns and optical coherence tomography. Retina 2012;32:1087–1099.
2. Antcliff RJ, Hussain AA, Marshall J. Hydraulic conductivity of fixed retinal tissue after sequential excimer laser ablation: barriers limiting fluid distribution and implications for cystoid macular edema. Arch Ophthalmol 2001;119:539–544.
3. Gass JDM. Stereoscopic Atlas of Macular Disease: Diagnosis and Treatment. St Louis, MO: Mosby; 1997:43–568.

Reply

To the Editor:

Thank you for your interest and thoughtful commentary on our article.[1] We agree that your plausible explanations for the development of diabetic macular edema (DME) may play a role. The synaptic portions of the outer plexiform layer is one of the most ischemic vulnerable tissues in retina, thus early barrier functional disturbances may exist in DME. Also, considering hard exudates usually accumulating in the Henle layer, it is possible that hyperosmotic materials (proteinous or lipidious) may predominantly accumulate in the outer plexiform layer and attract fluid from adjacent layers.

Many consider DME to be a complicated disease entity, consisting of at least two distinct clinical features (including treatment responses) of focal or diffuse edema. However, there have been too many opinions and controversies over them, thus, have caused much confusions to many ophthalmologists. We rather think that our "simplified" model will provide a main framework for understanding the pathoanatomy of DME.