

All of these subjects are being observed to 5 yr, and these data will be published when available.

Although we applaud the contributions of Avidan and colleagues to our understanding of the role of dementia in POCD, we encourage them to join us and the many other established research groups assessing POCD in conducting the rigorous prospective surgical trials necessary to provide conclusive answers. We also forcefully reject their assertion that our findings are meaningless. By focusing on our dichotomous categorization and virtually ignoring the fact that a continuous measure was also assessed, they are employing a strategy of misdirection that is unwarranted. In contrast to their mere "hope for truth," we have prospectively enrolled 394 patients to demonstrate that the APOE4 genotype is not associated with cognitive decline after noncardiac surgery.

David L. McDonagh, M.D.,* Joseph P. Mathew, M.D., William D. White, M.P.H., Mark F. Newman, M.D.

*Duke University Medical Center, Durham, North Carolina. david.mcdonagh@duke.edu

References

1. McDonagh DL, Mathew JP, White WD, Phillips-Bute B, Laskowitz DT, Podgoreanu MV, Newman MF, Neurologic Outcome Research Group: Cognitive function after major noncardiac surgery, apolipoprotein E4 genotype, and biomarkers of brain injury. *ANESTHESIOLOGY* 2010; 112:852-9
2. Avidan MS, Searleman AC, Storandt M, Barnett K, Vannucci A, Saager L, Xiong C, Grant EA, Kaiser D, Morris JC, Evers AS: Long-term cognitive decline in older subjects was not attributable to noncardiac surgery or major illness. *ANESTHESIOLOGY* 2009; 111:964-70
3. Winblad B, Palmer K, Kivipelto M, Jelic V, Fratiglioni L, Wahlund LO, Nordberg A, Bäckman L, Albert M, Almkvist O, Arai H, Basun H, Blennow K, de Leon M, DeCarli C, Erkinjuntti T, Giacobini E, Graff C, Hardy J, Jack C, Jorm A, Ritchie K, van Duijn C, Visser P, Petersen RC: Mild cognitive impairment—beyond controversies, towards a consensus: Report of the International Working Group on Mild Cognitive Impairment. *J Intern Med* 2004; 256:240-6
4. Gauthier S, Reisberg B, Zaudig M, Petersen RC, Ritchie K, Broich K, Belleville S, Brodaty H, Bennett D, Chertkow H, Cummings JL, de Leon M, Feldman H, Ganguli M, Hampel H, Scheltens P, Tierney MC, Whitehouse P, Winblad B, International Psychogeriatric Association Expert Conference on mild cognitive impairment: Mild cognitive impairment. *Lancet* 2006;367:1262-70

(Accepted for publication July 27, 2010.)

Permeability, Osmosis, and Edema

To the Editor:

I enjoyed the interesting article by Jungner *et al.*¹ on the effects of crystalloid *versus* albumin fluid resuscitation in rats

* "Osmotic pressure" is *not* a real physical pressure, but an effect due to the tendency of chemical systems to seek greater entropy. In thermodynamics, the potential that drives osmosis is referred to as "chemical potential."

with traumatic brain injury, and the excellent editorial by Dr. Drummond.² Thanks to these authors for highlighting the principles of osmosis that underlie the behavior of semi-permeable membranes, a key difference between peripheral and brain vasculature.

This letter is to note two typographical errors in a key part of the editorial that render the otherwise elegant explanations incorrect. The second paragraph explains the consequences of dilutional changes in colloid osmotic pressure (COP) in the periphery and in the brain. A key sentence states, "For example, a 50% reduction in COP produces a [small] transmembrane pressure gradient... but because small solvents move easily... fluid moves extravascularly and edema forms." This is incorrect as written; it should read, "because small *solutes* move easily." Shortly thereafter, the sentence describing the situation in the brain states, "With COP reduction, some transendothelial movement of water probably does occur, but dissolved solvent cannot follow and opposing osmolar and hydrostatic gradients develop immediately and measurable edema differences are prevented." Again, this should read, "dissolved *solute* cannot follow."

For readers less familiar with the physical chemistry, the explanation is this: A solvent (water) passes easily through a membrane, but an impermeant solute (colloid) does not. Because of an entropic effect, the solvent will diffuse into the compartment that has the higher concentration of the impermeant solute, *as if* it is acted upon by a physical driving pressure (the "osmotic pressure").* This is the phenomenon called osmosis. In our example, initially, the system is in equilibrium: the hydrostatic pressure inside the vessels exactly opposes the "osmotic pressure" due to intravascular colloid. In the next step, the colloid is diluted; now, the hydrostatic pressure overwhelms the opposing "osmotic pressure," and fluid extravasates.

Dr. Drummond's teaching point is that in the periphery, any reduction in colloid has a significant osmotic effect, because only the colloid is impermeant. The other *solutes*, small molecules such as electrolytes, pass freely through the membranes and therefore do not have an osmotic effect. In the brain, however, many solutes are impermeant (or diffuse only "with difficulty" [*i.e.*, to a small degree]). A reduction only in colloid will cause only a small reduction in the total osmotic effect. Therefore, as soon as a small amount of water has extravasated across the membrane (if any passes out at all), the balance of "osmotic pressure" and hydrostatic pressure is already restored.

There is an additional teaching point to make here: We may ask, how is it that only the colloid concentration, but not the small-solute concentration, changed with dilution in this example? The answer is two-fold: (1) The dilution was with crystalloid solution that contained small solutes of its own; and (2) the small solutes pass freely through the membranes elsewhere in the body, promptly equalizing the small-solute concentration (but not the colloid concentration) across the peripheral vasculature. The result-

ing solution, wherein only colloid concentration has changed, is what then enters the brain.

Again thanks to all for the beautiful demonstration of the relevance of physical chemistry to physiology!

Elana B. Lubit, M.D., Ph.D., New York University School of Medicine, New York, New York. elana.lubit@nyumc.org

References

1. Jungner M, Grände PO, Mattiasson G, Bentzer P: Effects on brain edema of crystalloid and albumin fluid resuscitation after brain trauma and hemorrhage in the rat. *ANESTHESIOLOGY* 2010; 112:1194–203
2. Drummond JC: Colloid osmotic pressure and the formation of posttraumatic cerebral edema. *ANESTHESIOLOGY* 2010; 112: 1079–81

(Accepted for publication August 10, 2010.)

In Reply:

I am grateful to Dr. Lubit for the kind words about the editorial¹ and for catching my slip. She is absolutely correct that in those two instances the intended word was solute rather than solvent.

John C. Drummond, M.D., F.R.C.P.C., University of California, San Diego, San Diego, California, and Veterans Affairs Medical Center, San Diego, California. jdrummond@ucsd.edu

Reference

1. Drummond JC: Colloid osmotic pressure and the formation of posttraumatic cerebral edema. *ANESTHESIOLOGY* 2010; 112: 1079–80

(Accepted for publication August 10, 2010.)