

Re: Mandhani A. The paradox of why and how in urology! Indian J Urol 2022;38:247-8

The editorial by Mandhani^[1] in the recent issue of the journal deserves praise for exhorting the urology community to dismantle the prevailing paradoxes with rational thinking and critical analyses. However, we believe that the virtuous appeal for innovation in urinary diversion surgery would have been more persuasive without the crutches of a fallacy; “nonabsorbable bladder mucosa.” The “nonabsorbable bladder mucosa” is a fallacy because the perusal of preclinical and clinical evidence published over the last six decades^[2-8] is enough to reject the null hypothesis with high confidence. Moreover, significant systemic uptake of instilled lidocaine and oxybutynin^[2,3] from the bladder lumen of healthy human volunteers in clinical trials buttresses the claim that the truth is indeed stranger than the fiction of “nonabsorbable bladder mucosa.”

It appears that the significance of a two-fold higher density of vasculature in mucosa over detrusor muscle^[4] needs to be better understood by the urology community so that misconceptions and myths do not get primetime coverage. While mucosal blood flow (9–17 cm/s) ensures significant systemic uptake of instilled drugs from the

bladder in clinical and *in vivo* studies, the absence of mucosal blood flow dramatically reduces the concentration gradient—the driving force of diffusion in *ex vivo* studies of mammalian bladder—which may have birthed the fallacy of “nonabsorbable bladder mucosa” and watertight bladder barrier. Studies on animals have now confirmed the aldosterone-sensitive active reabsorption of sodium ions,^[5,6] and dehydration-provoked reabsorption of urea and water through aquaporin channels across mammalian bladder mucosa for ensuring homeostasis. The preclinical findings were substantiated by the plasma recovery of instilled radiolabeled sodium^[7] and urea in human subjects. However, Eldrup *et al.*^[7] miscalculated the plasma recovery of <0.04% (absorbed dose fraction) for sodium and urea using plasma volume instead of the true volume of distribution (62% of body weight) for sodium as used for calculating the saline dose needed to correct hyponatremia. The role of disease or inflamed bladder mucosa in absorption was excluded by the systemic uptake ~5% of instilled permeability probe, ^{99m}Tc-diethylenetriaminepentaacetic acid,^[8] and >20% of instilled lidocaine^[2] and instilled oxybutynin^[3] by healthy human volunteers. In fact, the bioavailability

of lidocaine from the bladder was comparable to the same dose administered by subcutaneous injection^[2] and a cross-over trial demonstrated that the absence of first-pass effect from the bladder significantly raised the absorption of intravesical oxybutynin over oral oxybutynin.^[3]

The self-correcting nature of science is epitomized by the triumph of heliocentricity over egocentricity, as the support of empirical data for the former, a counter-intuitive concept, ultimately trumped over the support of sacred scriptures for the latter, the intuitive concept of the Earth being the center of the universe. By the same token, it is imperative to discard the intuitive dogma of “nonabsorbable bladder mucosa” for ensuring safe bladder instillation of lidocaine^[9] and antibiotics^[10] in the pediatric and vulnerable older populations, respectively.

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