Published in final edited form as:

Neurogastroenterol Motil. 2013 October ; 25(10): 854. doi:10.1111/nmo.12179.

Mucosal permeability testing: Should interpretation change or stay the same?

Danny S. Rafati, MD, PhD^{*,#,\$} and Robert J. Shulman, MD^{*,#,\$,†}

^{*}Department of Pediatrics, Houston, Texas

[#]Baylor College of Medicine, Houston, Texas

^{\$}Texas Children's Hospital, Houston, Texas

[†]Children's Nutrition Research Center, Houston, Texas

To the editors

We read with interest the paper by Sequeira *et al.*¹ The authors reported the temporal pattern of urinary excretion of mannitol and lactulose in smokers and nonsmokers in the presence and absence of aspirin, concluding that sampling methodologies may influence interpretation of results. Their data support our previous work demonstrating the temporal pattern of these, and other sugars used in gastrointestinal permeability testing.² Based on a previous study cited by Sequeira *et al.*, as well as their own data, the authors contend that the recovered quantities of individual sugars (i.e., mannitol) rather than the lactose to mannitol ratio (LMR) should form the basis for assessing permeability changes in the GI tract. While this is a provocative hypothesis, the available data cast significant doubt on the veracity of this contention. A large body of work has shown that mannitol absorption and subsequent urinary recovery is related to transit time, mucosal integrity, as well as surface area (the latter being the most important factor (see references 3 and 4, among others). Further, Elia *et al.*, among others, has shown that urinary recovery of intravenously administered mannitol and lactulose continues up to 24 hours after administration.⁵ Thus, urinary excretion of mannitol and lactulose is also dependent on renal clearance. Based on our data and theirs, we agree that interpretation of the LMR depends on the doses administered and the timing of the urine collection.¹⁻² That said, the wealth of studies demonstrating the utility of the LMR in evaluating small intestinal mucosal permeability (or damage) in inflammatory bowel disease, celiac disease, damage from nonsteroidal antiinflammatory drugs, allergic disease, environmental enteropathy, and following chemotherapy, as well as many other clinical conditions, underscores the utility of the LMR when used properly.

References

1. Sequeira IR, Lentle RG, Kruger MC, Hurst RD. The effect of aspirin and smoking on urinary excretion profiles of lactulose and mannitol in young women: toward a dynamic, aspirin augmented, test of gut mucosal permeability. *Neurogastroenterol Motil.* 2012 Sep; 24(9):e401-11. [PubMed: 22757650]
2. McOmber ME, Ou CN, Shulman RJ. Effects of timing, sex, and age on site-specific gastrointestinal permeability testing in children and adults. *J Pediatr Gastroenterol Nutr.* 2010; 50:269-275. [PubMed: 20081547]

3. Elia M, Behrens R, Northrop C, Wraight P, Neale G. Evaluation of mannitol, lactulose and ⁵¹Cr-labelled ethylenediaminetetra-acetate as markers of intestinal permeability in man. *Clin Sci (Lond)*. 1987 Aug; 73(2):197–204. [PubMed: 3115663]
4. Madsen JL, Scharff O, Rabøl A, Krogsgaard OW. Relationship between small-intestinal transit rate and intestinal absorption of (14)C-labelled mannitol and (51)Cr-labelled ethylenediaminetetraacetic acid in healthy subjects. *Scand J Gastroenterol*. 1996; 31:254–9. [PubMed: 8833355]
5. Dawson DJ, Loble RW, Burrows PC, Notman JA, Mahon M, Holmes R. Changes in jejunal permeability and passive permeation of sugars in intestinal biopsies in coeliac disease and Crohn's disease. *Clin Sci (Lond)*. 1988; 74:427–31. [PubMed: 3128419]