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**Creatinine based vancomycin dosing regimens in neonates:
there is more to consider than the variation in drug assay...**

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Creatinine based vancomycin dosing regimens in neonates: *there is more to consider than the variation in drug assay...*

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Dear editor,

With great interest we read the paper on the evaluation of vancomycin dosing regimens in preterm and term neonates by Mehrotra *et al.*¹ We fully agree that comparison of dosing regimens and prospective pharmacokinetic and –dynamic validation of dosing regimens in neonates are urgently needed.² However, we would like to draw the attention of the readers of this journal to the relevance of the analytical technique applied to quantify serum creatinine (Scr).³ Similar to the differences related to vancomycin quantification techniques mentioned by the authors, there are also significant differences in absolute values for Scr in neonates quantified by Jaffe or an enzymatic method.^{1,3} These differences in Scr quantification reflect the specific characteristics of neonates and relate to endogenous (e.g. bilirubin, hemoglobin F) and exogenous (e.g. penicillins) compounds that interfere with the Jaffe quantification technique.³

We recently reported on postnatal trends in Scr values in two consecutive cohorts of extremely low birth weight infants admitted to one single neonatal intensive care unit following a switch from the use of an uncompensated Jaffe to an enzymatic method to determine Scr.³ Clinical characteristics were similar and both cohorts had a similar Scr trend with a peak Scr on day 3-4 of life and a subsequent progressive decrease in the following 6 weeks. However, for all consecutive days, median Jaffe Scr values were significantly higher with a difference in median values for the consecutive days between 0.15-0.3mg/dl.³ Based on the threshold Scr values suggested by Mehrotra *et al.*, we assume that these Scr values are based on uncompensated Jaffe values and that similar Scr values following enzymatic quantification will likely be lower.^{1,3} Consequently, we strongly suggest that in prospective validation studies, the Scr quantification technique is another relevant covariate that needs consideration.

References

1. Mehrotra N, Tang L, Phelps SJ, Meibohm B. Evaluation of vancomycin dosing regimens in preterm and term neonates using Monte Carlo Simulations. Pharmacotherapy 2012, DOI 10.1002/j. 1875-9114.2012.01029.x.

2. Van den Anker JN. Getting the dose of vancomycin right in the neonate. Int J Clin Pharmacol Ther 2011;49:247-9.

3. Allegaert K, Kuppens M, Mekahli D, *et al.* Creatinine reference values in ELBW infants: impact of quantification by Jaffe or enzymatic method. J Matern Fetal Neonatal Med. 2012, DOI 10.3109/14767058.2012.657277.