Dear Sirs,

Gentamicin nephrotoxicity has been reported in patients with trough serum gentamicin values greater than 2 \( \mu g/ml \) [1]. Matthews and Chow feel that nephrotoxicity from gentamicin alone cannot be excluded in 2 of 4 patients reported by us [2] as the trough serum gentamicin value in each was 5 \( \mu g/ml \). We have studied 16 patients treated with gentamicin on 22 occasions [3] with dosages determined by creatinine clearance values and administered on an 8 hourly schedule [4]. The

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mean peak and trough serum gentamicin values were 6.4 and 3.6 µg/ml. For 17 courses of treatment, the creatinine clearance value was between 15 and 65 ml/min. Despite mean trough serum gentamicin values of greater than 2 µg/ml for 12 of 17 courses, there was a decrease in renal function in only 1 patient and this was clearly related to a hypotensive episode. The trough value was greater than 4 µg/ml during 6 courses of treatment and yet no patient suffered a deterioration in renal function. Dahlgren et al. [1] reported that renal function deteriorated in all 5 patients with a trough serum gentamicin value greater than 4 µg/ml. We cannot explain the discrepancy between our results and those of Dahlgren.

We agree that one cannot exclude a possible nephrotic effect of gentamicin alone but feel that the rapid development of renal insufficiency following addition of small doses of amphotericin B to 4 consecutive patients receiving gentamicin provides strong circumstantial evidence for synergistic action.

Although peak serum gentamicin values of 4-5 µg/ml are generally considered adequate for treatment of serious gram-negative sepsis, Riff [5] has suggested that patients with poor host defense mechanisms should have a sustained therapeutic serum gentamicin concentration, as long periods of sub-inhibitory levels are undesirable. Although there is no proven added effectiveness from sustained high serum gentamicin levels and there is a possibly increased toxicity, the relationship between therapeutic effect and toxicity deserves further prospective study.

David N. Churchill
The General Hospital and Memorial University of Newfoundland, St. John’s, Newfoundland (Canada)

John Seely
Division of Nephrology, Royal Victoria Hospital, McGill University, Montreal, P.Q. (Canada)

References