Lack of interaction between methotrexate and penicillins

Sir, We were interested to read the letter by Dawson and colleagues [1] drawing attention to reports suggesting that penicillins decrease the renal excretion of methotrexate or increase its toxicity. We first became interested in the possible interaction between penicillins and methotrexate after a patient with rheumatoid arthritis (RA) developed a methotrexate pneumonitis shortly after being prescribed flucloxacillin 2 g i.v. four times daily for an infected toe ulcer. We therefore undertook a pharmacokinetic study in 10 patients with RA on methotrexate therapy, to examine whether flucloxacillin might reduce methotrexate clearance [2]. Methotrexate pharmacokinetic profiles were obtained twice from each patient: in the presence and absence of flucloxacillin. We found a lower area under the curve for methotrexate in the presence of flucloxacillin (the opposite of what should have been observed had flucloxacillin reduced methotrexate clearance). Although this result was statistically significant, we did not feel that the reduced methotrexate levels with flucloxacillin were clinically relevant. We concluded that these findings suggested that in patients with RA there is no important pharmacokinetic interaction between methotrexate and flucloxacillin, although this does not exclude effects of flucloxacillin on the safety and efficacy of methotrexate through other mechanisms.

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