children undergoing intermittent hemodialysis (HD). Contrary to the recommendation from Robson et al [2] to dose after alternate HD sessions [2], we suggest to dose oseltamivir in children (age >1 year) after each HD session (7.5 mg for children weighing ≤15 kg, 10 mg for children weighing 16–23 kg, 15 mg for children weighing 24–40 kg, and 30 mg for children weighing >40 kg).

We have based this recommendation on 2 main arguments. First, dosing after alternate dialysis sessions leads to a low plasma concentration of oseltamivir carboxylate from the first HD session after the dosing until the next dosing, which is a period of ~48 h. Even though the total area under the curve is appropriate, the plasma concentration during this latter 48 h may be suboptimal. Second, safety analysis of oseltamivir has shown that high plasma concentrations are generally well tolerated [3] and may even be more effective than low concentrations [4].

To test our dosing schedule, plasma concentrations of oseltamivir carboxylate were measured using a validated liquid chromatography tandem mass spectrometry (LC-MS/MS) method (PRA International) in 3 children undergoing HD with suspected H1N1 infection. Blood samples, obtained from patients after a median of 2 days treatment, were taken just before and after an HD session to define extracorporeal elimination.

Results from the analysis are presented in Table 1. All patients recovered well, and none of the patients experienced any adverse effects as a result of the treatment. Our data show that plasma concentrations are attained at the lower end of an adult reference population [2] and that extracorporeal elimination is higher than expected (>80%).

We present the first data on oseltamivir dosing in children undergoing HD [5]. These data illustrate the appropriateness of our dosing schedule, and the high extracorporeal elimination indicates the need to supply a dose of oseltamivir after each HD session to prevent subsequent subtherapeutic exposure [2, 5]. Obviously, 3 patients are not enough to provide adequate evidence for our schedule, but in the clinical setting, we are confronted with children undergoing HD who need adequate and safe oseltamivir treatment. This forces us to define a dosing schedule on the basis of sparse data. We hope that more data will become available to define the best oseltamivir dosing schedule for this vulnerable patient cohort.

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Timely Administration of Antivirals for Pandemic (H1N1) 2009 Influenza

To the Editor—As part of a study on pandemic (H1N1) 2009 in patients hospitalized at our institution from 1 May through 30 June 2009, we evaluated antiviral prescribing practice and its timeliness. All study patients had positive test results for pandemic (H1N1) 2009 with use of an in-house reverse transcription polymerase chain reaction (RT-PCR), and
these results were confirmed by the Center for Disease Control and Prevention’s RT-PCR for pandemic (H1N1) 2009. This study was approved by the institutional review board of Rush University Medical Center.

There were 32 hospitalized patients, of which 16 were admitted to the intensive care unit (ICU). The most common diagnosis at hospital admission was pneumonia. Twenty-two (69%) of 32 patients received oseltamivir (44% of non-ICU vs 94% of ICU patients; P = .002). The median duration of symptoms prior to hospitalization was 3 days (range, 1–7 days). The median duration from hospitalization to the administration of oseltamivir was 27.3 h (range, 3.1–222.5 h). Among patients treated with oseltamivir, the median duration from the time the drug was ordered to the time it was administered was 3.5 h (range, 1.2–17.7 h). Ten (46%) of 22 patients had a delay of ≥4 h from the time oseltamivir was ordered to the time of administration.

Empiric treatment for pandemic (H1N1) 2009 influenza is currently recommended for all hospitalized patients with suspected or proven influenza [1]. Recent observations suggest a mortality benefit of antiviral treatment for hospitalized patients with 2009 (H1N1) influenza and recommend that treatment be initiated as early as possible in hospitalized patients [2, 3]. We observed a significant delay (median, 27.3 h) in the initiation of oseltamivir treatment among hospitalized patients. This may be attributable to delays in diagnosis or turnaround of RT-PCR results (batched and performed daily at our institution). More significant is that despite the use of an electronic medication order system, almost one-half of patients treated with oseltamivir experienced a delay of ≥4 h before receiving the drug. This may be attributable to the fact that orders for oral antivirals are not viewed with the same urgency as intravenous antibiotics, which can be ordered “stat.” The early administration of antibiotics has been demonstrated to have mortality benefit and is widely viewed as an important performance indicator [4]. The rapid initiation of antiviral therapy for influenza treatment should probably be viewed with similar importance [5]. The results of our study should encourage physicians, nurses, and pharmacists to examine closely all barriers to timely antiviral prescribing and administration.

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References


Emergence of Carbapenem-Resistant Hafnia: The Fall of the Last Soldier

To the Editor—Carbapenems, such as imipenem and meropenem, are recommended as first-line therapy for severe infections caused by cephalosporin-resistant Enterobacteriaceae. The emergence of carbapenem-resistant enterobacteria is therefore worrisome from a public health point of view because (1) the antimicrobial treatment options are very limited and (2) they may represent therapeutic dead ends, as novel treatments against gram-negative bacteria are not expected in the near future.

A 53-year-old male patient had a medical history of tuberculosis, fibromatosis, and chronic renal failure. Because of a peritoneal infection, he underwent abdominal surgery.

Strains of Hafnia alvei (H1), Enterobacter cloacae (E1), and Enterococcus faecalis were isolated from peroperative samples. The patient was treated with piperacillin-tazobactam after surgery, because H1, E1, and the E. faecalis isolates were susceptible. After 1 week, the patient became unstable and underwent surgery. Strains of H. alvei (H2) and E. cloacae (E2), both resistant to cephalosporins and piperacillin-tazobactam; an E. faecalis susceptible to ampicillin; and a mexitcillin-resistant coagulase-negative Staphylococcus were isolated, and the antibiotic therapy was changed to imipenem, vancomycin, gentamicin, and fluconazole. Twelve days later, a carbapenem-resistant H. alvei (H3) was isolated from a bronchoalveolar lavage sample and the therapy was changed to levofoxacin and gentamicin. Antibiotic resistance phenotypes and minimum inhibitory concentrations of carbapenems are presented in Table 1. Unfortunately, the patient died 2 weeks later with multiple organ failure and acute respiratory distress syndrome.

H1, H2, and H3, initially identified as H. alvei with use of API 20E strips, were then identified as belonging to the very recent Hafnia paralvei sp nov (formerly known as H. alvei DNA group 2) [1], by partial sequencing of RNA polymerase β-subunit (rpoB) and 16S ribosomal RNA genes. H1, H2, and H3 were indistinguish-