

positive PCR results were suspected of harboring B19 infection on the basis of clinical assessments [1]. Yet, retrospective review showed that the B19-associated cytopenias significantly prolonged periods of unwanted interruption of chemotherapy, necessitated more blood transfusions, and compelled more bone marrow examinations. Our purpose here was to extend those findings by studying children with other malignancies or hematological disorders.

During a period of 5.5 years, examinations of bone marrow for proven or suspected malignant disorders were supplemented with screening for parvovirus B19 DNA with a qualitative PCR. Positive samples were then analyzed with the quantitative PCR [1]. Informed consent to participate in the study was obtained from the children or their guardians. The study was approved by the ethical committee at Karolinska Institutet (Stockholm, Sweden).

A total of 229 bone marrow samples from 123 children who underwent bone marrow examinations were collected. Overall, 9 (7%) of 123 patients were positive for B19 DNA, and 8 of those 9 had test results positive for B19 DNA at the time of diagnosis of the underlying disease. No additional underlying immunodeficiency or previous blood transfusion was recorded. Consecutive samples were available from 4 of the B19 DNA-positive patients (2–7 samples per patient), and the outcomes were recorded for 5–32 months. B19 DNA was, in one instance, persistently detected for >24 months after diagnosis, and viral loads consisted of up to 8.7×10^7 copies/mL. According to a review of medical records, none of the B19 infections were suspected on clinical grounds, and the infections were not clustered during any given time of year or epidemic period. Serum samples that had been collected at the time of the first bone marrow sample collection were available from 27 of these children. Of these 27 children, 13 (48%) were B19 immunoglobulin

G positive, whereas only 1 was B19 immunoglobulin M positive. During the 6 months after diagnosis of the underlying disorder, all but 2 of the B19 DNA-positive patients experienced multiple episodes of fever and severe long-standing cytopenias that required multiple blood transfusions (range, 5–60 transfusions).

Except for studies involving children with ALL, little information is available on the influence and persistence of B19 infection among children with malignancies [1–6]. In the present study, 7% of children with malignant or hematological disorders were found to be B19 DNA positive and this infection likely contributed to some of the severe cytopenic periods observed. Viral load was detected in high titers, and some children had prolonged periods of detectable B19 DNA. Owing to the multiplicity of these underlying diagnoses, no statistical comparison was possible for B19-infected versus uninfected individuals, as was done in our previous study involving children with ALL [4]. However, that study served as the basis for our contention that screening with PCR for B19 DNA in bone marrow samples is clinically important for all children with malignancies, not only for early detection and treatment of the infection but also for limiting the effects of associated complications. Future studies will hopefully clarify the clinical relevance of viral load levels in different patient categories, at which levels to initiate antiviral treatment, and whether analyses of serum samples is as sensitive as analysis of bone marrow samples. Considering the notable number of B19 DNA-positive children in our relatively small but significant study, we suggest that quantitative PCR testing is a useful differential diagnostic tool in these patient categories.

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Oseltamivir Dosing in Children Undergoing Hemodialysis

TO THE EDITOR—With the advent of the new influenza A (H1N1) virus, the need for antiviral treatment has increased, especially in vulnerable patients, such as patients undergoing dialysis [1]. For adult patients, Robson et al [2] have provided a guideline for dosing of oseltamivir, whereas for children undergoing dialysis, such data are lacking.

On the basis of data from Robson et al [2], we formulated a dosing schedule for

Table 1. Characteristics of 3 Children undergoing Hemodialysis (HD) and Treated with Oseltamivir

Patient	Age, years	Sex	Body weight, kg	Diagnosis	Endogenous creatinine clearance, mL/min/1.73 m ²	HD treatment	Oseltamivir carboxylate plasma concentration before HD session, ng/mL	Oseltamivir carboxylate plasma concentration after HD session, ng/mL
A	3	M	15	Denys-Drash syndrome, bilateral nephrectomy	0	For 3 h 4 times per week; Fresenius F4HPS dialyser; effective blood-flow, 100 mL/min	660	133
B	6	M	24	Posterior urethral valves	5	For 3 h 3 times per week; Fresenius FX5 dialyser; effective bloodflow, 100 mL/min	207	37.3
C	11	F	34	Interstitial nephritis	2	For 4 h 3 times per week and for 3 h 1 time per week; Fresenius FX5 dialyser; bloodflow, 225 mL/min	419	60.7

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