

0.135 mg/L), with a maximum concentration 6 h after injection.

These values are in the low range, compared with previously reported ranges [1, 3]. In those 2 reports, information concerning liver function and the concomitant drugs received are not available. These low concentrations are similar to the MICs of the *Aspergillus* species and can explain the slow evolution of the abscess.

Three main explanations can be invoked for these low values. Pharmacokinetic interactions do not explain the low concentrations. With regard to the drugs the patient received, the interaction between tacrolimus and voriconazole leads to a higher concentration of tacrolimus and not to a lower concentration of voriconazole [4]. We did not find obvious interactions between voriconazole and prazosine, paroxetine, nicarpidine, or metopimazine.

We can assess that the liver graft was not involved in these low concentrations of voriconazole, because it exhibited normal function. The sampling procedure can perhaps explain the low results. The CSF specimen was collected during 2 h through the intraventricular catheter. Therefore, the in vitro instability of voriconazole and/or adsorption of voriconazole on the lines and collection materials of the intraventricular derivation are able to decrease measured CSF concentrations. Furthermore, we noticed in the previously reported data from Lutsar et al. [1] that, among samples that yielded the 7 lowest concentrations found (which were similar to ours), 4 samples were obtained through an intraventricular catheter. A nonhomogeneous distribution of voriconazole resulting from compression of the fourth ventricle could also explain the lower concentrations in ventricles, compared with the concentration expected from a lumbar puncture.

In conclusion, voriconazole is highly active against *Aspergillus* species, but additional studies are needed to confirm that our low drug concentrations result from

the method of sampling and not from poor efficacy of this molecule in the CSF.

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Use of Clinical Criteria and Molecular Diagnosis to More Effectively Monitor Patients Recovering after Severe Acute Respiratory Syndrome Coronavirus Infection

In early 2003, a novel severe acute respiratory syndrome (SARS) coronavirus (CoV) [1] spread around the world; ultimately, more than 8000 patients in 32 countries contracted SARS, many of whom died. Although gold standard methods, such as viral culture, can help diagnose SARS, these methods are by no

means as efficient and rapid as PCR-based diagnostic tests. The speed and sensitivity of molecular diagnostic tests for SARS is often considerably greater than that of serological and viral culture methods [2]. Our reported enhanced real-time PCR (ERT) method [3, 4] is ≥ 100 -fold more sensitive than conventional real-time PCR. The higher sensitivity of this method may reveal potential SARS CoV carriers who have SARS CoV levels that are undetectable by other methods, and the sensitivity of the ERT method may be particularly important for ensuring that patients who have had SARS are not infectious before discharge from the hospital [5].

In collaboration with Princess Margaret Hospital (PMH; Hong Kong), samples obtained from 3 patients during recovery after SARS were analyzed (table 1). Six to nine weeks after the onset of infection, SARS CoV could still be detected by ERT in certain samples (table 1), indicating that, although clinical signs and symptoms had subsided and a host immune response had been mounted, viral clearance was not complete. Patient 1 was transferred on 17 June 2003 to the Wong Tai Sin Hospital (WTSH; Hong Kong), which was converted into a specialized center for convalescent care of patients with SARS during the epidemic, but he was returned to PMH because of recurrent pneumothorax, indicated by chest radiography on 18 June. The ERT method clearly demonstrated the presence of SARS CoV in all samples obtained from the patient on 16 June (table 1), which was 1 day before his transfer to WTSH. The possible relapse of infection in patient 1 after his transfer to another hospital indeed raises the question of how patients with SARS who have PCR results negative for SARS CoV should be handled [5]. Standardization of clinical criteria and PCR-based methods should be emphasized to ensure accurate diagnosis of SARS after hospital admission and prior to hospital discharge. More studies will be necessary to determine the infectivity status of patients who have ERT results positive

Table 1. Summary of demographic characteristics, clinical history, and laboratory results for patients recovering after severe acute respiratory syndrome (SARS) coronavirus (CoV) infection in Hong Kong, 2003.

Variable	Patient 1	Patient 2	Patient 3
Sex	M	M	F
Age, years	49	86	87
Date of hospital admission	29 Mar	22 Mar	1 Apr
Symptoms	Allergy to penicillin and tetracycline; low-grade fever; sputum	Right MCA infarction; gouty attack; high-grade fever	Left corona radiata infarction; fever
Serological test result for SARS CoV	Positive	Positive	Positive
Radiographic findings	Bilateral infiltrates	RLZ hazz progressing to both lungs	Multiple patchy consolidations in both lungs
Date SARS confirmed	29 Mar	28 Apr	1 Jun
ERT results, by sample and date obtained			
NS			
16 Jun	Positive	Negative	Negative
24 Jun	Negative	Negative	Negative
27 Jun	Positive	Positive	Negative
02 Jul	Negative	Negative	Negative
OS			
16 Jun	Positive	Positive	Negative
24 Jun	Negative	Negative	Positive
27 Jun	Negative	Negative	Positive
02 Jul	Negative	Negative	Negative
Urine			
16 Jun	Positive	Negative	Positive
24 Jun	Positive	Negative	Negative
27 Jun	Negative	Negative	Negative
0-02 Jul	Negative	Negative	Negative
Stool			
16 Jun	Positive	Negative	Negative
24 Jun	Negative	Negative	Negative
27 Jun	Negative	Negative	Negative
02 Jul	Negative	Negative	Negative

NOTE. MCA, middle cerebral artery; NS, nasopharyngeal swab sample; OS, oral swab sample; RLZ hazz, right lower zone haziness.

for SARS CoV. The data suggest that medical professionals should verify whether residual viral particles present in recovering patients remain infectious and whether they may constitute the source of possible future outbreaks of infection.

Because SARS is a newly emerging disease that causes serious consequences, many countries have formulated contingency plans for possible future SARS outbreaks. One of the containment activities currently undertaken by the World Health Organization to prevent SARS from repeatedly becoming a widely established threat is to develop a robust and reliable

diagnostic test [6], which will probably rely on PCR-based technology. Use of a highly sensitive method, such as the ERT method [3, 4] and a similar method that was reported recently [7], will be the first step toward more accurate screening of suspected SARS carriers and will minimize the occurrence of false-negative cases. Patients with false-positive cases can always be quarantined while awaiting further reconfirmation of infection. But patients with false-negative cases could be discharged into the community and pose a dangerous SARS threat to the public [8]. Therefore, stringent clinical criteria and

use of the ERT method might effectively monitor patients recovering after SARS.

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