

Correspondence

Can We Describe the Epidemiology of Candidemia without Using Selective Blood Culture Bottles for Fungus Detection?

SIR—We recently read with interest the article by Marchetti et al. [1] about the epidemiology of candidemia in Swiss tertiary care hospitals. Candidemia is recognized as an increasingly common complication in hospitalized patients, not only in America, but also in Europe and Australia, where it is the fourth and fifth most common nosocomial bloodstream infection, respectively [2–5]. Marchetti et al. [1] observed during their survey (1) that the incidence of candidemia remained stable between 1991 and 2000, despite an increase in high-risk activities and (2) that no shift to azole-resistant *Candida* species was noted, despite a sharp increase in fluconazole use during the period studied. The diversity of blood culture methods used in the participating centers could limit the interpretation of such surveillance studies. Marchetti et al. [1] reported that only 7 (44%) of the 16 microbiology laboratories that participated in the survey used selective blood culture bottles for fungus detection. However, the use of selective fungal media could improve the rate of isolation of slow-growing, more fastidious *Candida* species [6]. Three major arguments support the use of selective fungal media, particularly for non-*albicans* species of *Candida*: a higher sensitivity, a reduced mean time for detection of yeast, and a longer incubation time than for selective media for aerobic and anaerobic organisms. In our experience, as well as in previous reports [6, 7], the experimental mean time to detection of growth of *Candida glabrata* when selective fungal vials for the Bactec Mycosis IC/F system (Becton Dickinson) are used ranges from

~19–21 h, compared with a mean time of 85–156 h when the Bactec Plus Aerobic/F system (Becton Dickinson) is used. A large retrospective study published in 2004 on 197 cases of fungemia diagnosed using Bactec Mycosis IC/F and Plus Aerobic/F media has completely confirmed these experimental data, highlighting a statistically significant reduction of the mean detection time associated with use of selective fungal vials [8]. A recent evaluation of an automated blood culture system also underlines the interest in specific media for the detection of mycobacteria and fungi (e.g., MB bottles for the BacT/Alert 3D system [bioMérieux] and Myco/F lytic bottles for the Bactec 9240 system [Becton Dickinson]) [9]. Selective fungal media are incubated for at least 6–7 days, according to the manufacturers' recommendations, but most of the laboratories specializing in mycology use longer incubation durations (i.e., up to 10–15 days for optimal detection of *Cryptococcus neoformans*). By contrast, it is now recognized that a 4-day incubation protocol for selective media for aerobic and anaerobic organisms allows a sensitivity of bacterial recovery of 99.94%, compared with the routinely used 5-day protocol.

Taken together, these data suggest that candidemia may remain undiagnosed because of lower sensitivity and shorter incubation protocol when only selective media for aerobic and anaerobic organisms are used, particularly in the case of *C. glabrata* infection. A description of the methods used for the diagnostic work-up of bloodstream infections due to *Candida* species appears to be a prerequisite for interpretation of the changing patterns of candidemia, and particularly for the surveillance of the emergence of infection with non-*albicans* species of *Candida*.

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Reply

SIR—We read with interest the letter by Tattevin et al. [1] questioning the validity of studies of candidemia epidemiology conducted without the use of selective blood culture bottles for fungus detection.

We fully agree that the detection of fungemia—as performed in most institutions today—is not optimal, and that the use of special methods would certainly improve both the time to and the rate of detection. In vitro and in vivo studies have indeed demonstrated an advantage of special media in favoring yeast growth (particularly that of *Candida glabrata*) or inhibiting concomitant bacteria in blood [2–5]. However, the systematic use of such media is expensive. Their selective use for patients at risk for candidemia is attractive, but this population is difficult to identify. In our institution, the majority of cases of fungemia were detected among patients for whom there was no special request for fungal blood cultures.

Tattevin et al. [1] claim that not using special fungal blood culture media could impede or delay the detection of some non-*albicans* species of *Candida*, such as *C. glabrata*. We have conducted a further analysis of the data published in our 10-year Swiss survey [6] to assess differences in the proportions of *Candida albicans* and non-*albicans* species of *Candida* (particularly *C. glabrata*) reported by the 7 laboratories using special fungal media and the 9 others using standard automated-monitoring blood culture systems. No difference was observed between the 2 groups of institutions nor in the ranking of *Candida* species among the most frequent bloodstream isolates. In addition, in one of the major hospitals participating in our study, use of special fungal blood culture bottles was introduced mid-survey with-

out leading to a higher detection of non-*albicans* species of *Candida* [7].

Time to detection, although very pertinent for patient management, has no influence on studies such as ours, which require only that the incubation time for blood culture is long enough (5–7 days) to allow the detection of almost all *Candida* isolates from blood cultures. In this type of study, the emphasis is on the number of cases of candidemia and not on the number of bottles that yield an isolate nor on the time to detection.

In this respect, it is interesting to note that, as in our report, none of the candidemia studies mentioned in the letter by Tattevin et al. [1] or referenced in our article [6] specify the type of blood culture bottle or system used or the duration of incubation. Moreover, even population-based prospective surveillance studies such as those of Kao et al. [8] and Trick et al. [9] do not mention how candidemia episodes were diagnosed, beyond the basic definition of 1 or more blood culture(s) positive for *Candida* species.

Thus, within the imperfections and variations in current laboratory practices, as well as patient selection, studies of the epidemiology of candidemia do offer useful information and can be compared. Interesting—and intriguing—differences in the incidence of candidemia and the distribution of *Candida* species are reported within and between continents, which should trigger further research regarding their origin.

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Risk Factors for Extrapulmonary Tuberculosis

SIR—We were surprised by the findings of Yang et al. [1] suggesting that female sex and non-Hispanic black race are risk fac-

tors for extrapulmonary tuberculosis, because traditionally, age, recentness of infection, and immune function are considered to be the main determinants of the clinical presentation of tuberculous disease. The reported association between Asian/Pacific Islander race/ethnicity and extrapulmonary disease may be confounded by immigration status. It would be interesting to read what proportion of the Asian/Pacific Islander subjects were immigrants and what proportion of the non-Hispanic black subjects were HIV positive, compared with the rest of the population.

In our experience at Jacobi Medical Center in the Bronx, New York, foreign-born patients contribute an increasing proportion of newly identified cases of tuberculosis. During 1999–2003, we identified 66 cases of tuberculosis, 33 of which occurred in foreign-born individuals from Africa, Asia, Europe, and Central and South America. In contrast, <10% of the subjects in the study by Yang et al. [1] were born outside of the United States. At least 18 of our 33 foreign-born patients were recent expatriates (i.e., they had been residing in the United States for <5 years before receiving a diagnosis of tuberculous disease) from countries with a high prevalence of tuberculosis. Recent expatriates were more than twice as likely to present with pulmonary disease than with extrapulmonary disease.

Of the 66 cases of tuberculosis, we identified 21 cases of extrapulmonary disease. Twelve of the 21 cases of extrapulmonary tuberculosis occurred in foreign-born individuals. We did not find a significant difference between patients with extrapulmonary tuberculosis and those with isolated pulmonary disease with regard to sex, HIV status, or age.

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Reply

STR—We thank Kohli and Jenny-Avital [1] for their comments on our article describing risk factors for extrapulmonary tuberculosis (TB) [2] and for sharing their findings. We were not surprised by the discrepancies between their findings and ours, given the considerable differences between the 2 studies with respect to sample design (hospital-based vs. population-based study), sample size (66 vs. 705 patients), and demographic characteristics of the study population (50% vs. 8% foreign-born patients).

We agree that the clinical presentation of tuberculosis can be affected by age, recentness of infection, and immune status. In our initial comparison, we observed that patients with extrapulmonary tuberculosis were, on average, younger than patients with pulmonary tuberculosis. However, after stratifying by sex, the difference in age was significant only among female patients. Thus, after adjustment for sex in the logistic regression model, we observed no age-related effect.

Kohli and Jenny-Avital [1] suggest that our findings of an association between extrapulmonary tuberculosis and race/ethnicity may be confounded by immigration status and potentially by HIV infection status. HIV infection status was available for ~36% of white patients and ~66% of non-Hispanic black patients in our study. The proportion of the HIV-positive patients was higher among non-Hispanic

black patients (6.94%) than among the other racial/ethnic groups (1.53%, 0%, and 5% for Hispanic patients, Asian/Pacific Islanders, and American Indians, respectively). After adjustment for sex, age, and race/ethnicity in a logistic regression model, HIV positivity was found to be strongly associated with extrapulmonary tuberculosis, but unknown HIV infection status was not. Our finding of an association between non-Hispanic black race/ethnicity and extrapulmonary tuberculosis is based on multivariate analysis using a logistic regression model, and the finding is consistent with the findings of earlier studies conducted with HIV-infected individuals [3, 4]. Furthermore, a recent population-based study conducted in Houston, Texas, that involved 1371 HIV-negative adults with tuberculosis found that white race was a significant protective factor for extrathoracic tuberculosis lymphadenitis, a common form of extrapulmonary tuberculosis [5]. In addition, this study demonstrated an increased risk of extrapulmonary tuberculosis among female subjects, an observation consistent with our findings.

We believe it is unlikely that the association with race/ethnicity results from confounding by immigration status. There were only 40 Asian/Pacific Islanders in our study sample. Most of them were from the Marshall Islands. Because of the small proportion of foreign-born patients in our study, it was not possible to assess the association between immigration status and tuberculosis disease presentation. Nevertheless, in the Houston study, which included a large number of immigrant patients, Southeast Asian and African origins, but not Mexican origin, were found to be associated with extrapulmonary tuberculosis.

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Effectiveness of Environmental and Infection Control Programs to Reduce Transmission of *Clostridium difficile*

SIR—The occurrence of *Clostridium difficile*-associated diarrhea (CDAD) has been related to exposure to antimicrobial and chemotherapeutic agents, gastrointestinal surgery or other gastrointestinal procedures, and old age [1]. Such exposure alters the composition of the normal gut microflora, allowing *C. difficile* overgrowth and elaboration of toxins within the colon [2]. A variety of environmental sites within institutions, such as commodes (toilets), bathing tubs, and elec-

tronic thermometers, have been found to be contaminated with *C. difficile* spores. Efforts to prevent and control the spread of *C. difficile* with hypochlorite solution were effective when infection rates exceeded 3 cases per 1000 patient-days in the bone marrow transplant (BMT) unit at Barnes-Jewish Hospital (St. Louis, MO) [3]. This study provides follow-up regarding the combined infection and environmental control programs to reduce *C. difficile* transmission in 2 geographic units in the same university-based hospital (Barnes-Jewish Hospital).

At our institution, the incidence of CDAD increased from 3.9 cases per 1000 patient-days (1 January 2001 through 31 December 2001) to 5.8 cases per 1000 patient-days (1 January 2002 through 30 June 2002) in the medical intensive care unit (MICU) ($P = .20$), and from 6.7 cases per 1000 patient-days (1 January 2001 to 31 December 2001) to 8 cases per 1000 patient-days (1 January 2002 through 31 July 2002) in the BMT unit ($P = .32$). To compare the incidence of CDAD before and after the implementation of infection control and environmental control programs in the BMT and the MICU, a retrospective cohort study was performed to observe the trend in CDAD before and after intervention. Environmental and infection control programs were implemented from 1 July 2002 through 31 August 2002 in the MICU and from 1 June 2002 through 30 July 2002 in the BMT unit. Infection control interventions included educating the staff regarding contact isolation, having the staff wear gloves and gowns, and posting hand-washing signs. Environmental control programs included daily cleaning and disinfection of patient rooms and staff work and lounge areas with unbuffered 1:10 hypochlorite solution. Carpeted areas were also cleaned. Cleaning of patient rooms and environmental areas with unbuffered 1:10 hypochlorite solution was discontinued on 31 August 2002 in the MICU but was continued in the BMT unit.

After the intervention, the incidence of CDAD decreased to 2.1 cases per 1000 patient-days (31 July 2002 through 30 November 2002) in the MICU ($P = .05$) and to 4.2 cases per 1000 patient-days (30 August 2002 through 30 November 2002) in the BMT unit ($P = .04$). The differences in CDAD rates in both units after the intervention were considered significant and suggested a trend toward improvement in CDAD rates. This 50% reduction in CDAD rates in both units persisted for 12 months after the interventions. There were no significant changes in patterns of antibiotic use or in the antibiotic control programs in either unit during the study period. The surveillance programs for *C. difficile* detection were continued in both units.

Several barrier methods have been used at different institutions to protect patients from acquisition of *C. difficile* infection, with varying success. The successful methods have included the use of disposable gloves and thermometers, implementation of contact isolation, and the cohorting of infected patients [4–8]. Several studies emphasized the role of environmental control in interrupting an outbreak [3, 7, 9], highlighting the importance of environmental cleaning and disinfection of patient rooms and medical equipment. Our report confirms the effectiveness of both infection control and environmental control programs to reduce the environmental burden and decrease the transmission of *C. difficile* among susceptible patients.

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The Incidence of *Clostridium difficile*-Associated and Non-*C. difficile*-Associated Diarrhea after Use of Gatifloxacin and Levofloxacin in an Acute-Care Facility

SIR—We read with great interest the recent report by Gaynes et al. [1]. We would

like to share a similar but somewhat different observation from our hospital. Levofloxacin was the quinolone of choice in our hospital formulary until July 2001, when gatifloxacin was introduced. We have observed an increase in the incidence of diarrhea and in the number of requests for *Clostridium difficile* toxin assays after gatifloxacin became the quinolone of choice. A study was initiated with the purpose of determining whether gatifloxacin was more likely to promote *C. difficile*-associated diarrhea (CDAD) than was levofloxacin. Here, we briefly summarize our findings.

The study was conducted in Coney Island Hospital, an acute-care community hospital of ~350 beds located in South Brooklyn, New York. This was a retrospective study that involved chart review of the patients admitted to our inpatient department from July 1999 through June 2002. From a computer record of our inpatient pharmacy, the medical record numbers of 400 patients who received levofloxacin and of another 400 patients who received gatifloxacin were randomly selected. The computer records for each of these patients were reviewed for age, sex, date of hospital admission, length of hospital stay, date on which antibiotic (levofloxacin or gatifloxacin) therapy was started, date on which a *C. difficile* toxin assay was requested, result of the toxin assay, and length of therapy. The date of the *C. difficile* toxin assay request was defined as the date of development of diarrhea. Cases of diarrhea that developed within 48 h after admission were excluded from analysis because we did not know what the predisposing factors were. Cases of diarrhea that developed after 24 h and within 6 weeks after initiation of therapy with 1 of these 2 antibiotics were included in analysis. Inconclusive results of the *C. difficile* toxin assay were considered to be negative. For patients who developed CDAD, charts were reviewed for use of other antibiotics, both for concurrent use and use within the previous 6-week pe-

riod. Findings were compared for statistical significance using the χ^2 test.

Table 1 contains data on the mean age, the ratio of male to female subjects, the average duration of therapy, and the length of hospital stay. There was no significant difference between the levofloxacin group and the gatifloxacin group with regard to these parameters. A total of 47 patients (11.75%) in the levofloxacin group and 74 patients (18.5%) in the gatifloxacin group developed diarrhea for which a toxin assay was requested; the difference was significant ($P = .01$). There were more patients in the gatifloxacin group than in the levofloxacin group (8 vs. 4) who had a positive result of the toxin assay, but this difference was not statistically significant ($P > .05$). A total of 4 patients in the gatifloxacin group had an inconclusive toxin assay result. Among the patients with proven CDAD, there were no differences in the duration of therapy, length of hospital stay, and use of other antibiotics in either group (data not shown), although the mean age of patients with CDAD in the gatifloxacin group was greater (74 vs. 56 years).

Beginning with a case report in 1989 [2], there have been a number of publications associating quinolone use with CDAD [3–5]. The study by Gaynes et al. [1] and our study are the only reports, to our knowledge, that compared 2 quinolones with regard to their association with CDAD. Both of these studies found a higher incidence of diarrhea after use of gatifloxacin than after use of levofloxacin. There are 2 main differences in the findings of these 2 studies. In our study, although a large number of patients developed diarrhea after use of gatifloxacin (18.5%) and levofloxacin (11.75%), the actual incidence of proven cases of CDAD was low (2% and 1% for gatifloxacin and levofloxacin, respectively). The difference was not statistically significant, probably because of the relatively small number of positive cases. A possible reason for the low incidence of CDAD could be the nature of the population. The study by Gay-

Table 1. Characteristics of the patients who received a course of quinolone antibiotics and who developed diarrhea.

Characteristic	Levofloxacin recipients (n = 400)	Gatifloxacin recipients (n = 400)	P
Age, mean years	65	69	...
Sex, % of patients			
Male	44	41	...
Female	56	59	
Duration of therapy, mean days	4.3	5.4	...
Duration of hospital stay, mean days	11.4	9.6	...
No. (%) of patients who developed diarrhea	47 (11.75)	74 (18.5)	.01
<i>Clostridium difficile</i> assay performed, no. (%) of patients			
Underwent testing	42 (10.5)	52 (13)	>.05
Positive result	4 (1)	8 (2)	>.05

nes et al. [1] was done at a long-term care facility, where the length of stay is much longer; our patients were treated in an acute-care hospital, where the length of hospital stay is shorter (table 1). Because of the retrospective nature of our study, we do not have data on any patient who may have developed diarrhea after discharge from the hospital. An additional factor may be the more strictly followed infection-control measures in an acute-care facility, compared with a long-term care facility. The second finding of our study is that a significantly higher percentage of patients developed non-CDAD in the gatifloxacin arm than in the levofloxacin arm. The cases of diarrhea that developed in gatifloxacin recipients appeared to be self-limiting and of short duration. Thus, a significantly lower number of *C. difficile* toxin assays were actually performed in the gatifloxacin recipients who developed diarrhea (52 [70%] of 74) than in the levofloxacin group (42 [89%] of 47). Gatifloxacin has enhanced activity against many anaerobic bacteria [6, 7]. Whether this property of gatifloxacin is associated with development of diarrhea by a mechanism other than the overgrowth of toxin-producing *C. difficile* in the colon remains to be explained.

We conclude that the incidence of diarrhea is significantly higher after use of gatifloxacin than after use of levofloxacin.

However, most of these cases are not CDAD.

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Pharmacokinetics of Voriconazole in the Cerebrospinal Fluid of an Immunocompromised Patient with a Brain Abscess Due to *Aspergillus fumigatus*

SIR—In a recent article, Lutsar et al. [1] reported voriconazole concentrations in the CSF. We report our experience. A 51-year-old woman with a liver graft was given voriconazole for a brain abscess due to *Aspergillus fumigatus*. External ventricular drainage was performed for compression of the fourth ventricle. On the basis of NCCLS breakpoints, the *A. spergillus* species was susceptible to voriconazole (MIC, 0.125 mg/mL) [2]. The patient received intravenous voriconazole (200 mg b.i.d., adjusted to her weight [40 kg]) after a dosing charge. With this treatment, the volume of the abscess slowly decreased, as noted on CT scans during follow-up.

Because we had easy access to CSF specimens as a result of the external ventricular drainage, we measured the concentration of voriconazole in the CSF on day 11 after the course of voriconazole therapy was started. Voriconazole concentrations were measured 2, 4, 6, 8, 10, and 12 h after the commencement of intravenous administration. CSF samples were obtained via the external ventricular drainage and were immediately frozen at -20°C until analysis. The assays were performed using high-performance liquid chromatography coupled with a diode array detector method, as described elsewhere [1]. At the time of sampling, the patient had also been receiving prazosine, paroxetine, nicarbidine, metopimazine, and tacrolimus for several weeks. The CSF concentrations of voriconazole were 0.08–0.17 mg/L (median,

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, nicaripidine, 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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