Prolonged norovirus shedding and the use of a rapid norovirus polymerase chain reaction to assess terminal room cleaning in immunocompromised patients

Sir

Noroviruses have been recognized as an important cause of chronic gastroenteritis in immunocompromised patients [1–4]. Prolonged norovirus illness has been reported in persons who are immunosuppressed as a result of immunosuppressive therapy [1]. Norovirus shedding in stool has been detected by polymerase chain reaction (PCR) for up to 56 days in immunocompetent patients [2]. In immunocompromised patients this can be longer; Ludwig *et al*. reported norovirus detection up to 433 days in paediatric cancer patients [3]. Roddie *et al*. reported that 18% of patients who underwent allogeneic hematopoietic stem-cell transplantation contracted norovirus over a one-year period [4]. Here we describe ongoing transmission of norovirus GII from a chronic carrier on a clinical haematology ward at Queen Elizabeth Hospital, Birmingham (QEHB), UK. We also describe the use of a norovirus PCR to assess for environmental clearance of the virus.

A patient with acute myeloid leukaemia was admitted to the clinical haematology unit at QEHB in January 2018 due to manifestations of graft versus host disease. During this admission, the patient acquired norovirus GII due to an outbreak on the ward, and was then isolated in a single room. The patient subsequently had multiple stays on the ward during these 10 months (five inpatient stays in total), during which time he had persistent diarrhoea and continued to test positive for norovirus by PCR. On each admission the patient was isolated in a different side room (either balanced pressure or positive pressure) with en-suite toilet facilities, and on discharge an infectious clean of the room was routinely undertaken.

However, despite these measures a total of 14 patients acquired confirmed norovirus GII infection during the times that this patient was on the ward. Additionally, three staff members developed norovirus-like illnesses, although these cases did not undergo norovirus PCR testing. Epidemiological data indicated that the chronic carrier was the only common factor on each occasion, suggesting this was the index patient for these transmissions. In two instances the patient immediately admitted into the room vacated by the index patient acquired norovirus infection. Molecular typing also suggested transmission of the same strain of norovirus (GII genotype 4 prototype strain Sydney/2012/Australia).

In response to the evidence of ongoing transmission from the chronic carrier, in October 2018 the positive pressure side room that had been occupied by the chronic carrier patient for 29 days was environmentally sampled post-discharge. Before sampling the room underwent enhanced cleaning, comprising detergent/disinfectant (1000 ppm; Chlor-Clean, Guest Medical, Aylesford, UK), steam-cleaning, and double-strength hypochlorite solution (2000 ppm; Chlor Clean) followed by hydrogen peroxide misting (OxyPharm, Sandbach, UK) at 12% concentration. After cleaning was assessed as adequate by an infection-control nurse, multiple macroscopically clean touchpoints throughout the side room were then sampled (Table I), as described previously [5]. Swabs were tested using the Cepheid Xpert Norovirus PCR (Cepheid Inc, Sunnyvale, CA, USA) [6]. Norovirus was detected by PCR from the environmental sampling after the enhanced clean. A second room clean was ordered, which included an additional step of ultraviolet irradiation (Hygiene Solutions, Kings Lynn, UK) (Table I). This time, no detectable norovirus was detected on environmental sampling and the bed space was reopened.

Table I
Norovirus polymerase chain reaction results from environmental sampling of seven surfaces in the patient's room using polywipe sponges (surface area ~30 cm^2)

Surface tested	Enhanced clean – norovirus PCR result	Enhanced Clean with ultraviolet – norovirus PCR result
Surface areas in the vicinity of the patient		
Bed frame	+	–
Table	+	–
Cardiac monitor	–	–
Floor	–	–
Communal area surfaces tested		
Bathroom handles	+	–
Door handles	–	–
Fridge	+	–

+, positive polymerase chain reaction (PCR) for norovirus; –, negative PCR for norovirus. The enhanced room clean comprised of a detergent/disinfectant (1,000ppm; Chlor Clean), steam-cleaning, double-strength hypochlorite solution (2000 ppm; Chlor Clean) followed by hydrogen peroxide misting (OxyPharm) at 12% concentration. The only difference with the enhanced clean with UV irradiation was the addition of UV (Hygiene Solutions, UK) after the enhanced clean of the side room.

In immunocompromised adults, norovirus gastroenteritis can become chronic and persist for weeks to years [1], as in the case described here at QEHB. Bok *et al* suggested that it is not clear whether noroviruses are transmissible to immunocompetent adults from patients with chronic viral shedding, questioning the virulence of noroviruses in this setting [1]. However, in our experience we saw secondary cases throughout a chronic carrier's inpatient stays over a 10-month period, probably including immunocompetent staff members.

Prior room occupancy is the single biggest risk factor for acquiring healthcare associated micro-organisms [7]. Using a norovirus PCR to assess the environment after cleaning may be an important tool in providing assurance that it is safe to admit patients into bed spaces previously occupied by norovirus shedders.

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None declared.

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Concerns regarding the validity of the conclusion in a recently published paper on Roche Liat implementation

Sir,

We have read the publication by Youngs *et al.* with great interest [1]. As molecular-based point-of-care infectious disease diagnostics are currently being implemented widely, data regarding the usability of these tests at the point-of-care setting are highly warranted. We are however, concerned about the validity of the main conclusion of the study, claiming a low sensitivity (85.4%) of the Roche Liat Influenza A/B and RSV assay for influenza A/B compared to Fast Track Diagnostics respiratory pathogens 21 multiplex assay.

First, this finding is in conflict with previously published studies, which report an excellent sensitivity by Liat Influenza A/B testing (97.9%–100.0%) [2–6], and the authors do not offer any explanation for this finding besides an 'increased risk of errors such as testing the wrong sample because of transcription errors or poor use of the equipment by non-laboratory staff'. Although this concern should be addressed as part of quality control of any routine point-of-care implementation, the authors did not address this issue, e.g. by re-testing all Liat point-of-care tested samples by Liat in a laboratory setting.

Second, the study protocol called for a differentiated re-testing of Liat-positive and Liat-negative samples; only 29.9% of Liat-positive samples were re-tested by either Fast Track respiratory pathogens 21 multiplex or Cepheid Xpert Xpress Flu/RSV assays, whereas 83.9% of Liat-negative samples were re-tested by Fast Track respiratory pathogens 21 multiplex assay. This lack of an established gold standard compromises calculations of sensitivity and specificity and complicates comparison with other reported studies. It also creates a selection bias that increases the chance of discordant results for Liat-negative samples because a much higher proportion of negatives are re-tested and therefore included in the analysis.

Third, and most importantly, no discrepancy testing was performed. Since all 15 false-negative Liat results were detected with high Ct values in the Fast Track respiratory pathogens 21 multiplex assay, the results could also be regarded as false positive by Fast Track respiratory pathogens 21 multiplex assay. As variations between different NAT tests at the lower end of the detection ranges are well known, calculating sensitivities and specificities in the absence of a discrepancy test makes little or no sense. Especially considering the findings of all other published studies of the Liat Influenza A/B and RSV assay, which found excellent sensitivity, robust discrepancy testing is critical and the assumption in the publication by Youngs *et al.* that the routine laboratory reference is correct is problematic [1].