Lipoarabinomannan point-of-care tests: evaluation with fresh samples needed

Tobias Broger and colleagues[1] reported an evaluation of a urine point-of-care test for tuberculosis targeting lipoarabinomannan. The authors tested frozen specimens retrieved from a biorepository and acknowledged that a limitation of their study was the potential difference in analytical performance between frozen and fresh urine samples.

We investigated the effect of freezing on lipoarabinomannan concentrations of unprocessed patient urine. We measured the concentration of lipoarabinomannan in urine samples (n=15) before and after freezing to –70°C in polyethylene terephthalate tubes using an in-house ELISA. Samples were frozen for a minimum of 1 day before being retested. The mean lipoarabinomannan concentration decreased from 138 pg/mL (SD 99) to 76 pg/mL (SD 77), while the average loss was 50%. These results indicate that fresh samples contain more detectable lipoarabinomannan, which might improve the sensitivity of the described test. The use of fresh samples might be most crucial in patients expected to have low lipoarabinomannan concentrations, such as those with a CD4 count higher than 200 cells per µL.

Depending on the handling of urine before and after freezing, differences in protein content and pH can be dramatic—urine alkalises over time,[2] and protein content can drop after a freeze–thaw.[3] These factors could affect performance of lateral flow tests by eliminating some of the variability between urine samples, leading the assay developer to produce a less robust test, unable to handle the spectrum of fresh urine. This could yield a high rate of false positivity.[4,5]

On the basis of our results and the crucial changes in urine with freezing,[2,3] we conclude that the difference between fresh and frozen urine samples is a non-trivial matter.

We declare no competing interests.

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1 Broger T, Sossen B, du Toit E, et al. Novel lipoarabinomannan point-of-care tuberculosis test for people with HIV: a diagnostic accuracy study. *Lancet Infect Dis* 2019; **19:** 852–61.
2 Cook JD, Strauss KA, Caplan YH, LoDico CP, Bush DM. Urine pH: effects of time and temperature after collection. *J Anal Toxicol* 2007; **31:** 486–96.
3 Brinkman JW, de Zeeuw D, Duker JJ, et al. Falsely low urinary albumin concentrations after prolonged frozen storage of urine samples. *Clin Chem* 2005; **51:** 2181–83.
4 Brown MC. Antibodies: key to a robust lateral flow immunoassay. In: Wong RC, Tse HY, eds. Lateral flow immunoassay. New York: Humana Press, 2009: 59–74.
5 Hsieh HV, Dantzler JL, Weigl BH. Analytical tools to improve optimization procedures for lateral flow assays. *Diagnostics* 2017; **7:** 1–14.

Vaccine against Middle East respiratory syndrome coronavirus

In *The Lancet Infectious Diseases*, Kayvon Modjarrad and colleagues[1] reported results of the first in-human clinical trial of the GLS-5300 vaccine candidate against Middle East respiratory syndrome (MERS) coronavirus. The vaccine induced both humoral and cellular MERS coronavirus-specific immune responses. These data suggest that GLS-5300 has potential value in protecting humans from MERS coronavirus infections. However, who should be vaccinated?

Epidemiological surveys[2] concluded that camel contacts, healthcare workers, and patient household contacts are high-risk groups. Therefore, they should be the target groups for the vaccine. However, there are many infection cases for which the source of infection could not be identified. The unpredictability of these infections makes it hard to prevent human infections through vaccination for postexposure prophylaxis.

For zoonotic disease prevention and control, one-sided disease prevention (either human or animal) is often inefficient. Severe acute respiratory syndrome (SARS) is a successful precedent for containment of emerging coronaviruses based on elimination of the primary reservoir. Although the pathogens of SARS and MERS are both coronaviruses, two major factors lead to different control results. First, although the number of human SARS cases is greater than for MERS, most were due to a so-called super-spreader strain. By contrast, all clades of MERS coronavirus are shared by camels and humans, indicating that MERS coronavirus can easily spill-over from camels to infect humans.[3] Second, palm civet, the intermediate amplifying host of SARS coronavirus, is an exotic animal that could easily be controlled by banning wild animal trading. However, the intermediate host of MERS coronavirus (dromedary camel) is an important livestock for the Middle East, with key roles in transportation, food, and fabric (wool); thus, it is impossible to eliminate all camels.

To control this disease in camels two possibilities exist: mass slaughtering of infected animals or vaccination. Unfortunately, serological surveys showed a very high prevalence (up to 100%) of MERS coronavirus-neutralising antibodies in dromedary camels.[4] Therefore, it seems impossible to eliminate this disease by mass slaughtering of positive animals. Vaccination of camels seems to be the only choice, but no licensed vaccine for camels is currently available, although several vaccines are in development.[5] Additionally, GLS-5300 has been reported to also be immunogenic in camels.[6] Camels are not used routinely in research and, for most laboratories, it would be hard to attain enough animals and work with them. Moreover, they