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Improved standardization and potential for shortened time to results with BD Kiestra™ total laboratory automation of early urine cultures: A prospective comparison with manual processing

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ABSTRACT

We compared the results of 505 urine specimens prospectively processed by both conventional manual processing (MP) with 16–24 h incubation to BD Kiestra™ Total Laboratory Automation (TLA) system with a shortened incubation of 14 h: 97% of culture results were clinically concordant. TLA processing was associated with improved standardization of time of first culture reading and total incubation time.

1. Introduction

Recently, instruments for automation of microbiology sample inoculation, streaking, and incubation have become available. However, few peer-reviewed publications exist that evaluate the potential clinical benefits of such instruments. In particular, publications studying the benefits of automation of the entire bacteriology process are scarce (Dumitrescu et al. 2011; Greub and Prod'hom 2011; Mulatero et al. 2011). The need for "objective, comparative, and preferably prospective clinical studies" of this new technology has been recognized and such studies are necessary to define the true, rather than perceived or hoped-for, value of total laboratory automation (TLA) in clinical microbiology (Doern 2013).

One of these platforms, the BD Kiestra™ Total laboratory Automation (TLA) system is equipped with digital image reading that allows uninterrupted incubation time therefore potentially detecting growth at an earlier time. Theoretically, this has the potential to reduce result turnaround time, improve laboratory workflow and decrease laboratory workload.

A small number of studies have demonstrated that instruments for automated sample inoculation produce satisfactory reproducibility and may improve microbiological endpoints (such as colony recovery and isolation) compared to manual inoculation. For the BD Kiestra™ InoqulA component of the TLA, these studies were mainly performed on mock samples or on a small number of varied clinical sample types (Froment et al. 2014; Mutters et al. 2014; Croxatto et al. 2015), or with comparisons made to retrospective data (Strauss and Bourbeau 2015). Since the magnitude of the impact of TLA benefits may vary by specimen type these evaluations should ideally be performed separately. One study, supported by BD Kiestra, has compared this instrument to the Copan WASP^R for urine samples incubated for a conventional 18 h and found that the InoqulA gave more accurate quantitative results (Iversen et al. 2016).

In this study, we aimed to prospectively compare the performance of BD Kiestra™ TLA to MP for a large number of urine specimens. Clinically meaningful parameters such as the categorical interpretation of the culture result and turnaround time (TAT) were evaluated. In addition, we studied the impact of TLA on standardization of incubation time and whether the shortening of this time altered the culture result.

2. Materials and methods

Monash Pathology Microbiology laboratory is a 24-h laboratory that services outpatients and a large healthcare network with over 2000 acute and sub-acute inpatient beds in Victoria, Australia. Consecutive urine specimens received on four weekdays between 0800 and 2100 h were prospectively processed by both conventional MP, and by BD Kiestra™ TLA (BD Kiestra B.V., JC Drachten, The Netherlands). All non-invasively collected urine specimen types received were included in the study including indwelling catheter urines and clean catch urines.

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For urines processed by TLA, 10 μL of specimen was inoculated onto a split Horse Blood agar/MacConkey agar plate (HBA/MAC, Thermo Fisher Scientific, Australia) and incubated for 24 h at 35 °C in an aerobic incubator. All plates were digitally imaged by the Kiestra™ system at 14, 16, 18 and 24 h. TLA setup was performed by one of four microbiologists/technicians. All TLA images were read by one of two study investigators (LT, RS) who were at the time blinded to the result of the manual culture results. For TLA culture, reading was performed by counting the colonies on the image. Urine culture results by both MP and TLA method were categorized into one of 7 categories designated A to G (Table 1). Due to the difference in inoculum used, for Manual processing "No growth" was $<10^6$ CFU/L but for TLA "No growth" was $<10^5$ CFU/L.

For the conventional MP, the laboratory standard operating procedures were for all urines to be inoculated with 1 μL calibrated loop onto a Brilliance UTI Clarity plate (BUC; Thermo Fisher Scientific, Australia) and incubated at 35 °C in an aerobic incubator for 16–24 h. Subsequently, microscopy was performed and if urine microscopy demonstrated ++ or greater bacteria per high power field, a split HBA/MAC was also inoculated and incubated at 35 °C for 16–24 h. If urine microscopy demonstrated ++ or greater bacteria per high power field, and there was no growth, or fine growth on the first reading at 16–24 h, the HBA/MAC plate was to be re-incubated for a further 24 h. If yeast were detected on microscopy, a Brilliance™ Candida Agar (Thermo Fisher Scientific, Australia) was also inoculated.

After category designation for each specimen was recorded for both MP and TLA, any specimens with discrepant results had review of TLA and MP culture plates by study investigators (LT, RS). If the reviewed result was different to the reported result, then this was also recorded.

2.1. Definitions

MP first read TAT: time from specimen inoculation to time culture plates first read. The time of first reading of culture plates is automatically recorded by the laboratory information system (LIS) if the scientist enters information into the LIS at that time.

MP first result TAT: time from specimen inoculation to time a result was first entered into culture field in LIS.

TLA TAT: time from specimen inoculation to time digital image captured.

Time to inoculation: time from specimen registration to inoculation of plates.

Clinically discrepant: specimens for which the categorical reporting would indicate clinically different results that may result in a difference in treatment.

Microbiologically discrepant but clinically concordant: specimens for which the reported results would be unlikely to lead to a difference in treatment. For example, category B and category E would both only have susceptibility results reported for one organism.

3. Results

A total of 505 urines were processed by both MP and TLA and were imaged at 14 h, 16 h, 18 h and 24 h by TLA. Urine specimen types are summarized in Table 2 and include: midstream urine specimen ($n = 248$), indwelling catheter urine specimen (20), clean catch (Greub and Prod'hom 2011), indwelling suprapubic catheter (Dumitrescu et al. 2011) and method of collection not stated (234). Out of 505 urine specimens cultured, 255 had no growth and 36 specimens had pure growth of $\geq 10^7$ CFU/L of a uropathogen, with 23 of these being *Escherichia coli* (Table 2).

Table 3 summarizes the specimens with clinically discrepant culture results by TLA and MP methods. Only 15 specimens had clinically discrepant culture category designation, indicating a concordance of 97%. For the 15 clinically discrepant urine results, the most common cause for discrepancy was greater growth on the TLA cultures: either the colony count was greater or the number of different colony types was greater for most of the TLA urines. Only one out of the 15 urine specimens had lower number of colony types on TLA processing compared to MP: on review of the MP cultures, 3 colony types were obvious on the BUC plate but only two colony types were obvious on review of the TLA images (including the 24 h TLA image). Five urine specimens had no growth with MP, but 10–100 colonies (10^6–10^7 CFU/L) with TLA, which is considered low colony count and would only be reported with susceptibility results for invasively collected urine specimens or if the request slip indicated a symptomatic female or prostatitis. We have conservatively categorized these urine specimens as "clinically discrepant" although they would be considered concordant in many clinical scenarios (Strauss and Bourbeau 2015; UK Standards for Microbiology Investigations 2014).

Table 4 summarizes the specimens with microbiologically discrepant but clinically concordant results between TLA 14 h and MP. The most common cause for discrepancy was also greater growth on the TLA cultures. However, there were ten specimens categorized as "no significant growth" on MP which had no growth on TLA at 14 h: 6 of these specimens remained as no growth at TLA 24 h incubation but the other 4 specimens had low colony counts.

We found that 181 urine cultures had a MP first result TAT of less than 16 h and for these specimens, the mean MP first result TAT was 14.0 h (standard deviation [SD], 1.4 h). 91 of these 181 specimens had ≤10 white cells (WC) on microscopy with no growth on MP and a further 25 specimens had 11–100 WC with no growth. 19 specimens had positive culture with further workup of identified organisms, and 39

Table 1
Definitions – Culture results category**.

No. of cultured isolates	Colony count – CFU/liter (CFU/L)	Category
0	No growth*	No growth
1	10^5–10^7 CFU/L for TLA 10^6–10^7 CFU/L for MP	A
1	$\geq 10^7$ CFU/L	B
2	Both 10^6–10^7 CFU/L	C
2	Both $\geq 10^7$ CFU/L	D
2	1 10^6–10^7 CFU/L 1 $\geq 10^7$ CFU/L	E#
≥3 none predominant^	Any	F
≥3 one predominant^	Any	G

** Culture result interpretation based on reference (UK Standards for Microbiology Investigations 2014).

* Due to the difference in inoculum used, for Manual processing "No growth" was $<10^6$ CFU/L but for TLA "No growth" was $<10^5$ CFU/L.

Only isolate with $>10^7$ CFU/L would have susceptibility testing performed as per reference (UK Standards for Microbiology Investigations 2014).

^ Predominant isolate defined as isolate with number of colonies 10 times greater than all other colony types.

Table 2
Culture results by MP.

Culture category	Number of urine specimens in this category by MP	Details of growth
No growth	255	
A	1	
B	36	23 *E. coli* 5 *Klebsiella pneumoniae/oxytoca* 1 *Enterobacter aerogenes* 1 *Citrobacter koseri* 3 *Proteus mirabilis* 1 *Streptococcus agalactiae* 2 *Enterococcus sp.*
C	0	
D	6	
E	1	
F	195	174 No significant growth^ 21 Mixed growth (MG)
G	11	

^ No significant growth if all isolates $<10^7$ CFU/L.