

Current State of Laboratory Automation in Clinical Microbiology Laboratory

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BACKGROUND: Although it has been 30 years since the first automation systems were introduced in the microbiology laboratory, total laboratory automation (TLA) has only recently been recognized as a valuable component of the laboratory. A growing number of publications illustrate the potential impact of automation. TLA can improve standardization, increase laboratory efficiency, increase workplace safety, and reduce long-term costs.

CONTENT: This review provides a preview of the current state of automation in clinical microbiology and covers the main developments during the last years. We describe the available hardware systems (that range from single function devices to multifunction workstations) and the challenging alterations on workflow and organization of the laboratory that have to be implemented to optimize automation.

SUMMARY: Despite the many advantages in efficiency, productivity, and timeliness that automation offers, it is not without new and unique challenges. For every advantage that laboratory automation provides, there are similar challenges that a laboratory must face. Change management strategies should be used to lead to a successful implementation. TLA represents, moreover, a substantial initial investment. Nevertheless, if properly approached, there are a number of important benefits that can be achieved through implementation of automation in the clinical microbiology laboratory. Future developments in the field of automation will likely focus on image analysis and artificial intelligence improvements. Patient care, however, should remain the epicenter of all future directions and there will always be a need for clinical microbiology expertise to interpret the complex clinical and laboratory information.

Introduction

Automation is the technology by which a procedure is performed without human assistance or intervention. In the laboratory context, automation refers to the switch from manual work to machines (1). In clinical microbiology culture, however, “full laboratory automation” refers to automation of the diagnostic workflow including all steps from inoculation to final report. Therefore, a laboratory automation system can potentially contribute to all analytical steps from inoculation, incubation, plate reading and identification, or even antibiotic susceptibility testing (1, 2).

While automation has been steadily spreading throughout the clinical chemistry and clinical hematology laboratories, until recently most processes for culture-based testing in the clinical microbiology laboratory have been performed manually (3, 4). The introduction of automation in microbiology was considered difficult to apply for several reasons such as the complexity and variability of sample types, the variations of specimens processing, the doubtful cost-effectiveness especially for small and average-sized laboratories, and the perception that machines could not exercise the critical decision-making skills required to process microbiological samples (2, 5, 6).

It was only toward the end of the 20th century that the concept of automating the laboratory process in clinical microbiology became a topic of interest (5, 7, 8). Despite the substantial barriers, healthcare and clinical laboratory trends mandated a change in the clinical microbiology landscape. Increasing pressure to reduce costs while maintaining or improving quality created a demand for automation. At the same time, technological advances converged to bring total laboratory automation (TLA) to microbiology (3, 7). Of the primary drivers for this change, standardization of identification methods with MALDI–TOF–MS and the adoption of liquid microbiology specimen transport created a workflow pattern that could be optimized with automation (5). At the same time, overall testing volumes have been increasing 5%–10% every year, driven by an aging population (5, 6), increased numbers of immunocompromised patients, infection control demands, and the growing challenge resulting from detection of multidrug-resistant microorganisms. Despite this volume increase, the available workforce of microbiology-trained personnel and the

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clinical laboratory training programs have been decreasing over time (3, 5, 9).

The first semiautomated plating instrument, the IsoplaterTM (Vista Technology, Edmonton, Alberta, Canada), was developed in 1989. Since then, other more sophisticated plating instruments have been developed, such as the InnovaTM (BD), the InoqulaTM (part of the TLA system of BD KiestraTM), the Walk-Away Specimen Processor (WASP)TM (Copan Diagnostics), and the Previ IsolaTM (bioMérieux) (2, 6, 10).

The goals of this review are to provide an overview of the current state of automation in clinical microbiology and report the main developments in recent years. We present the available hardware systems (that range from single function devices to multifunction workstations) and the challenging alterations to workflow and organization of the laboratory that must be implemented in order to optimize automation. We discuss some of the practical considerations that a laboratory might face during the automation implementation process. It is out of the scope of this review to cover developments related to nucleic acid amplification tests or automation of cultures other than bacteria.

Description of Laboratory Automation Systems

Laboratory automation consists of 2 components: the hardware and the workflow. In this section, we define terms commonly used when it comes to automation in clinical microbiology and present the key components of a TLA system (1).

TERMS

Hardware. Hardware defines all the components and physical parts of the devices used in the diagnostic process of the laboratory. Depending on the level of automation, someone might find systems (hardware) capable of performing only specific tasks (for example inoculation, incubation) or more sophisticated systems able to provide a higher level of automation.

Workflow. Workflow refers to a repeatable pattern of activity performed by a person, a machine, or a combination of both. It is used for short or long sequences of operations. The whole process involving a patient's sample, from arrival to the end of the diagnostic procedure, can be described as a sequence of workflows.

Software. Software includes the automation interface with the user to review the digital images, document and transmit results from the user, and storage of digital images. Additionally, automated image interpretation and artificial intelligence tools are included in the definition of software.

Time to report. It refers to the time necessary from sample's arrival to dispatch the result. It corresponds to the interval between the start and the end of a workflow or a combination of workflows. This may also be referred to as turnaround time.

Quality. The term quality can be described as a measure of excellence and uniformity. It is a performance metric for following established standards to obtain results without any significant variations (1). In laboratory practice, quality may refer to laboratory-based preanalytic errors (e.g., mislabeling plates, selecting incorrect media, misplacing a plate), quality of plate streaking, and ability to recover a microorganism (e.g., taking into account the number of isolated colonies, accurate quantification, the need to perform subcultures) or reproducibility (3, 11–13).

Total laboratory automation (TLA). TLA is used for reference to systems that are capable of automating the workflow of processing specimens, inoculation of broths, slides and agar plates, and imaging of culture plates.

MAIN COMPONENTS OF A CULTURE-BASED TLA SYSTEM

Currently, there are only a few companies offering complete laboratory automation systems for microbiology laboratories: BD Kiestra (USA) and CopanTM (Italy). Beckman Coulter with the DxA 5000TM (USA) and i2a Diagnostics with RECITALSTM (France) are 2 companies that provide compact solutions for portions of the automation process. Technical features, advantages, and disadvantages of the major automation systems have been extensively detailed elsewhere (1, 2, 6, 10, 14). It is out of the scope of this review to provide a comparison of those systems. Rather, we will provide an overview of the main components needed for the composition of a TLA unit with a brief description of existing technologies in the market for each corresponding hardware.

Inoculation/streaking unit. Most fully automated streaking systems require liquid transport swabs or liquid samples. Specimens can be loaded into racks and then onto the instrument for proceeding. Plates are then inoculated and streaked depending on what is specified for a particular pattern (2, 3). This involves de/recapping specimen containers, precise handling of liquids, and opening/closing culture plates. Streaking units can streak between 140 and 400 plates per hour and stock up to 24 different media. The most common specimen processors are the BD Kiestra InoqulaTM (USA), the Copan WASP DTTM (Italy), the ALIFAX SidecarTM (Italy), the Beckman Coulter DxM Autoplak systemTM (USA), the i2a Diagnostics PreluDTM (France), and the Sener diagnostics AutoplakTM (Spain).

Incubation system and high-resolution imaging. Incubators in microbiology need to provide a favorable environment for growth of microorganisms, such as maintenance of optimal temperature and atmosphere. Of note, at this time, automated systems do not have anaerobic incubators or other specialized incubation conditions for specific organisms (i.e., microaerophilic conditions for *Campylobacter* spp.) and, accordingly, anaerobic culture plates must be incubated outside of the system (3). Incubators in a TLA system must also have robotics that enable movement of plates within the incubator so that specific plates can be accessed, discarded, or photographed on demand. Photography modules are often adjacent to or a component of the incubator. Digital photography allows the use of multiple colors and lighting conditions, customization of the time interval of picture taking, and elimination of variations in background. BD Kiestra TLA and WCATM, Copan WASPLabTM, and i2a MaestroTM enable automated specimen processing, plate incubation, and digital imaging.

Several manufacturers have developed artificial intelligence and image analysis algorithms for computer-assisted culture interpretation, which enables successful identification and report of plates showing no significant growth, colony recognition, or even efficient identification of microorganisms based on chromogenic media. Copan PhenoMATRIXTM (15–18), Clever Culture Systems APAS IndependenceTM (19), and Rapidmicro biosystems Growth Direct SystemTM (20) are some major systems offering digital culture's interpretation. Studies evaluating image analysis systems for detection of organisms from chromogenic media have shown an increased sensitivity for detection of organisms from chromogenic media in routine screening for pathogens of infection control significance such as methicillin-resistant *Staphylococcus aureus* (21), Vancomycin resistant *Enterococcus* (22), and carbapenem-resistant *Enterobacteriaceae* (23). Two studies evaluated the performance of chromogenic media plus image analysis systems compared to molecular detection of Group A *Streptococcus* (17, 24) from throat specimens and Group B *Streptococcus* (15) from vaginal–rectal swabs in pregnancy screening. Both studies demonstrated improved sensitivity using the image analysis system that approaches, but did not reach, the sensitivity of molecular assays. Even on nonchromogenic media, image analysis systems sensitive and specific image recognition software have been able to categorize cultures by growth and no growth cultures and characterize the growth in the culture by organism classification or morphology (16, 18).

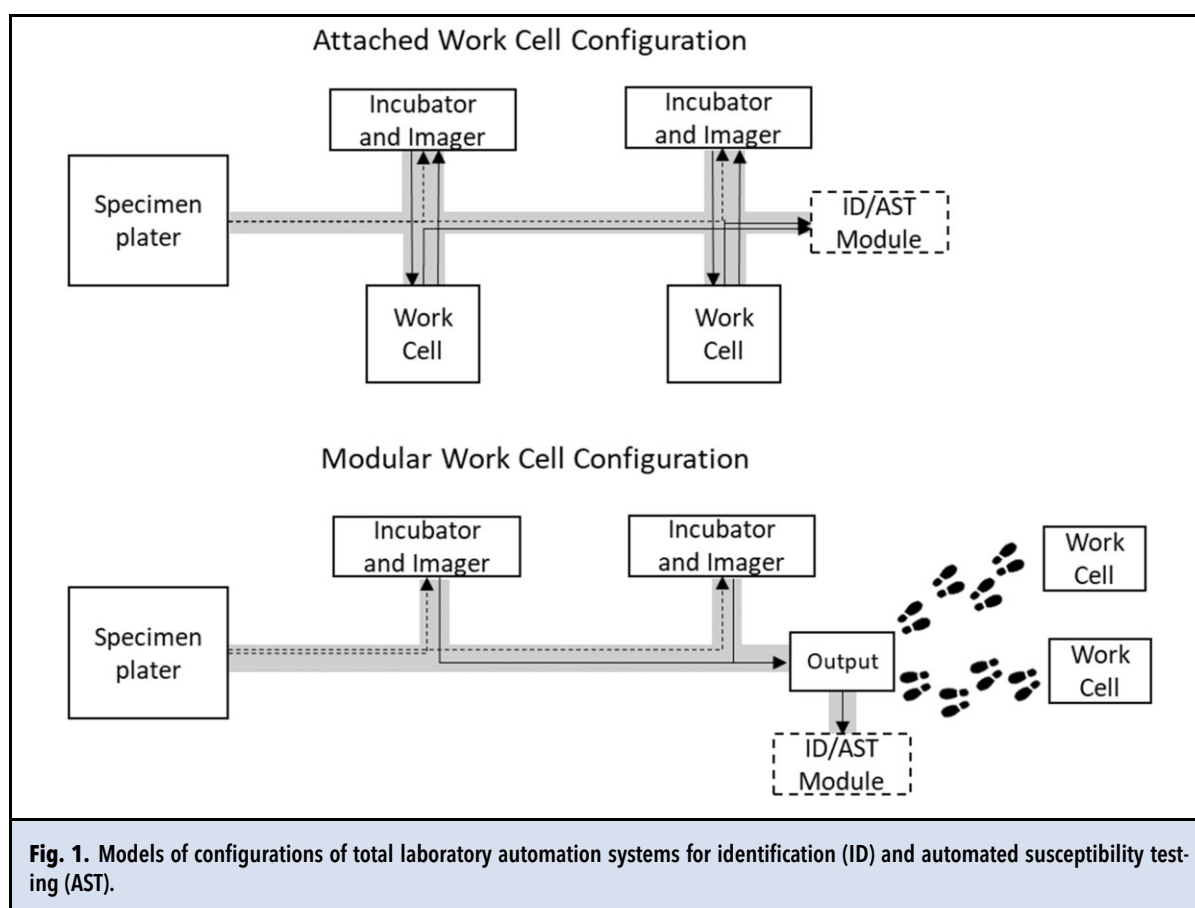
Postimaging analysis (workstations). TLA systems have relocated technologists from the traditional

microbiology benchtop to a plate-reading workstation, also called telebacteriology. Within a workstation, multiple images can be viewed simultaneously so that a technologist can correlate growth patterns across multiple light settings and different media types or multiple time points for a given specimen. The technologist can further decide whether a plate will be held for further investigation or if it will be discarded. Generally, the monitor used for the workstation should meet specifications provided by the manufacturer to ensure appropriate resolution and color differentiation for accurate culture reading.

Organization of the Laboratory

The decision to move to TLA is typically associated with a major shift in laboratory workflow and management. Implementation of TLA in the microbiology laboratory allows not only technological innovation, but also brings the necessity for innovative approaches to the organization of the laboratory. The clinical microbiology laboratory has traditionally operated with independent work-up benches using a one or 2 shift model for plate reading. With the implementation of automation systems for plating, incubation, and imaging, there are opportunities for changes in both the physical and personnel organization of the laboratory.

Generally, there are 2 approaches to the organization of the automation system in the laboratory, an attached work cell or modular work cell approach (Fig. 1). In the attached work cell systems, all stations from plating, imaging, and work-up are attached via a conveyor belt system. Specimen plates are transported to the incubator, imaged, and called out to the technologist via this conveyor belt. The technologist can perform the necessary work-up at their work station and return the plates and subsequent subcultures to the incubator, if necessary, via the conveyor belt system. In a modular work cell format, the specimen plater and incubation/imaging systems are typically attached to the line. The work-up stations are located separate from the automation line. When technologists identify cultures that need additional manual work-up, specimens are called out from the incubator and sent to an output module where the technologist retrieve the specimens and return them to their work station. Automation systems that incorporate plating, incubation, and work-up have options for either attached or detached work stations and the laboratory will have to determine which meets the needs of their local setting. Systems that provide individual pieces of automation (i.e., plating only or imaging only) may be incorporated into a modular work cell or potentially connected through universal conveyor belt systems to create a more attached work cell system.



Traditionally clinical microbiology does not operate using a 24-h schedule for culture reading and interpretation. If laboratories are operating 24 h, generally only culture plating and Gram stains are performed during the overnight hours. Automation of the front-end plating systems allows for nonspecialists to load samples onto the automation system for plating to provide 24-hour plating of specimens in the laboratory (25). However, this shift in plating over 24 h requires that laboratories examine when they have technologists available to read cultures based on a 24-h or shorter incubation schedule (Table 1). Laboratories may also consider if they continue to organize the benches based on culture type (i.e., urine bench, wound bench) or generalize the bench assignment based on time ready to read.

All these potential changes have a large impact on the organization and workflow of the laboratory, and come with distinct advantages and disadvantages that will be unique to each laboratory system (Table 2). Factors influencing these changes may be if a laboratory is within a hospital or part of a consolidated laboratory system, the staffing that is available, local regulatory requirements, and local labor law requirements.

Automation offers more than just efficiency in current processes. The way to truly capitalize on the value offered by automation is to evaluate every current process and determine whether and how it should change.

Benefits of Laboratory Automation in Clinical Microbiology

Laboratory automation has gained much interest during the past decade with a growing number of publications evaluating the potential impact in the clinical microbiology laboratory. The benefits the most well studied in recent publications represent:

- improved standardization (enhanced quality and reproducibility of bacterial cultures)
- increased laboratory efficiency (reduced turnaround times) and higher productivity
- increased workplace safety
- reduced long-term costs

Table 3 summarizes the most common benefits that have been reported. Of note, a few of those studies

Table 1. Advantages and disadvantages of various options in implementation of total laboratory automation. TAT (turnaround time).			
Options		Advantages	Disadvantages
Work cell configuration	Attached work cell	All functions contained within system Gained efficiency	Requires significant contiguous laboratory space May not support future expansion Requires complex conveyor belt systems
	Modular work cell	Requires less contiguous space Modular and can grow in future	Technologists have to retrieve and return plates from system
Culture reading shifts	Limited culture reading hours	Maintain current staffing schedules	Will result in delayed TAT for culture results
	24-h culture reading	Optimizes TAT and efficiency gained by automation	Changes to staff schedules Additional cost of overnight staffing should be considered
Culture reading organization	By culture type	Maintain current training and competency assignment	Limits the value of using automation to increase efficiency
	By ready to read	All cultures can be read by any staff when the image is captured Increases efficiency and improves turnaround time	Staff may have to be trained on additional benches
Implementation	Staged implementation	Opportunity to slowly deploy portions of the system	May take longer or stall completely to achieve full implementation
	Complete implementation	All sections of the laboratory gain the efficiencies of automation	More change management required Barriers impacting implementation of a section of the line may delay

Table 2. Factors to consider prior to implementation of total laboratory automation system.

Items to consider when implementing a laboratory automation system	
Space	Does the laboratory have the existing physical space to install the automated system or will construction be required? Is there enough space to conduct both automation and manual processes while the system is being installed and validated? Is there space to maintain some additional manual process instrumentation in the event of automation downtime?
Staffing	Will staffing schedules change, will work be performed on extended hours? How will training and competency on the automation system be managed? Do staff need to be trained on additional work benches or tasks not previously performed?
Performance	How will you conduct the validation of the automation system? What is the throughput of the instrument and imaging system? What is the quality of the instrument camera and reading monitors?
Maintenance	What is required for routine maintenance (i.e., daily, weekly, monthly, annual)? How often does the instrument require unscheduled maintenance? How quickly are maintenance issues resolved and do service engineers have to be sent to the laboratory?
Cost	Is the laboratory able to justify the cost of the system? What are the costs of consumables? What is the cost of the annual service contract? Is there labor savings expected due to increased efficiency, how will that be measured?

draw attention to potential drawbacks related with TLA. A later section in this review raises this specific question and addresses the challenges related to the management change and TLA implementation.

IMPROVED STANDARDIZATION

Standardization and reproducibility are 2 crucial issues in laboratory diagnostics. Initial efforts made after the introduction of laboratory automation in clinical microbiology have been essentially focused on comparing the quality of automated versus manual processing. Studies assessing the quality of isolation and productivity of automated systems have consistently reported higher yield of discrete colonies or colony distribution and separation (14, 26–31). In a prospective comparison in 2014 of the fully automated Inoqula (BD Kiestra) system versus the manual method, there was a higher quality of isolation with the automated method (27). Those data were confirmed over a year (14) in a prospective comparison of automated inoculation with the Inoqula (BD Kiestra) and the WASP (Copan, Italy) against manual inoculation. A 3- to 10-fold higher yield of discrete colonies was observed with automated inoculation. This difference was mainly observed at bacterial concentrations above 10^6 bacteria/mL. Another study (28)

evaluated quality metrics of urine clinical specimens before and after installation of the Inoqula (BD Kiestra) automation system in 2015. The Inoqula instrument improved quality and standardization of the isolation of bacterial cultures.

Some of these improvements may result from the use of flocked swabs instead of standard swabs on the automated systems. A comparative study in 2011 (26) evaluated the sensitivity of automated culture of *Staphylococcus aureus* from flocked swabs (using the Walk-Away Specimen Processor, Copan, Italy) versus that of manual culture of fiber swabs from nasal swabs. The automated culture significantly increased the detection rate by 13.1% for direct cultures and by 10.2% for enrichment cultures. The combination of automation and flocked swabs, significantly improved the recovery of organisms and can potentially result in improved diagnostic accuracy.

Another important characteristic of laboratory automation is its ability to enhance the recovery of fastidious microorganisms (32, 33). This feature is likely due to the fact that cultivation of microorganisms in TLA system incubators decreases time from inoculation to incubation, maintains a standard temperature due to the contained incubation system, and limits the exposure of

Table 3. Recent studies summarizing the most common benefits of automation.

Reference	Type of study	Type of sample	Studied outcome	Summary of main results
Cherkaoui et al. (26)	Retrospective comparison of pre- and postimplementation periods of the WASPLab system.	Urine specimens. Screening ESswabs of MRSA, VRE, and ESBL.	TAT from reception of samples to delivery of the culture results.	• Decrease in median TAT for negative reports (from 52.1 h to 28.3 h for urine, $P < 0.001$ and from 50.7 to 26.3 h for MRSA ESswabs, $P < 0.001$). • Decrease in median TAT but less pronounced for screening of ESBL and VRE ($P < 0.001$). • No significant change in the median TAT for positive samples.
Bailey et al. (27)	Comparison of 2 different time points to capture the first photograph of urine culture plates (18 h vs 16 h) using the BD Kiestra TLA system.	Urine specimens.	TAT to final results for positive cultures.	• Significant decrease in time to final results for positive cultures (71.6 h median time for the 18 h timepoint vs 61 h for the 16 h timepoint). • Slight decrease in sensitivity ranging from 2% to 7% (depending on the species) for the 16 h timepoint.
Yarbrough et al. (28)	Comparison of pre- and postimplementation periods of BD Kiestra TLA system.	Urine specimens.	TAT for major processing steps and result reporting.	• Increased TAT from receipt to inoculation (23 min vs 32 min postautomation, $P < 0.001$) and total processing time (28 min vs 66 min postautomation, $P < 0.0001$). • No change in time to identification or
<i>Continued</i>				

Reference	Type of study	Type of sample	Studied outcome	Summary of main results
				susceptibility results. Decrease in TAT to final report (from 43.8 h to 42 h post-automation, attributed mainly to decrease in TAT of negative results, $P = 0.02$).
Choi et al. (29)	Prospective comparison of manual versus automated streaking with Previ Isola system.	Clinical blood cultures. Urine specimens.	Consistency of bacterial growth between the 2 methods. Quantity of colony counts. Sample processing time (preparation and streaking time).	- High concordance rate in terms of quality and quantity among the 2 methods. - Previ Isola demonstrated lower hands-on-time for inoculation per sample.
Theparee et al. (30)	Retrospective comparison of pre- and postimplementation periods of the BD Kiestra TLA + MALDI-TOF MS.	Urine specimens.	TAT to identification. TAT to antibiotic susceptibility. TAT to final report.	- Decrease in time to identification (18.5 to 16.9 h) - Decrease in time to AST results (41.8 to 40.8 h) - Decrease in time to report for negative cultures (17.7 to 13.6 h) ($p > 0.001$).
De Socio et al. (24)	Retrospective comparison of 8 h incubation and digital plate imaging with BD Kiestra Work Cell Automation system vs an overnight incubation period.	Mono-microbial positive blood cultures.	TAT to identification. TAT to antibiotic susceptibility testing. Duration of empiric antibiotic therapy.	- Significant reduction of time to results ($P > 0.001$) with the 8 h incubation method. - Significant reduction of duration of empirical therapy ($P < 0.001$) and 30-day crude mortality rate ($P < 0.037$).
Graham et al. (23)	Prospective comparison of BD Kiestra	Urine specimens.		Improved standardization of time of
Continued				

Reference	Type of study	Type of sample	Studied outcome	Summary of main results
	TLA vs manual method.		TAT from inoculation to first culture reading. Total incubation time.	first culture reading and total incubation time. No difference in time from specimen inoculation to time a result was entered in LIS.
Quiblier et al. (20)	Prospective head-to-head comparison of the fully automated WASPLab workflow (Copan, Italy) versus manual processing.	Urine specimens.	Quality of isolation (number of single colonies, number of detected morphologies, and recovered species). Culture positivity rates.	- Similar positivity rates between the 2 methods. - Automated processing resulted in higher quality isolation in compare to the manual method in terms of single colonies yielded (for 32.2% of the samples), detected morphologies (for 47.5% of the samples), species (for 17.4% of the samples) and pathogens (for 3.4% of the samples).
Strauss et al. ^a (17)	Comparison of pre- and postinstallation periods of Inoqula (BD Kiestra).	Urine specimens.	Culture positivity rates. Quality of isolation. TAT to final identification. TAT to antibiotic susceptibility testing.	- Improved quality and standardization of the isolation with Inoqula instrument. - Shorter TAT to identification during automation period for negative results ($P < 0.001$). - Slightly higher TAT to identification for positive cultures with 2 results reported with only one of them reported with BD Phoenix ($P = 0.04$).
<i>Continued</i>				

Reference	Type of study	Type of sample	Studied outcome	Summary of main results
				No difference in TAT to antibiotic susceptibility testing during the 2 periods.
Croxatto et al. (14)	Prospective comparison of the automated inoculation with InoqulA (BD Kiestra) and the Walk-Away Specimen Processor (WASP, Copan, Italy) with manual inoculation.	Mono- and polymicrobial bacterial suspensions. Urine specimens.	Yield of discrete colonies and colony distribution. Reproducibility of each inoculation system to produce discrete colonies. Requirement to perform additional reisolation.	A 3- to 10-fold higher yield of discrete colonies was observed with automated inoculation than with manual inoculation (difference mainly observed at concentrations $>10^6$ bacteria/mL).
Mutters et al. (25)	Comparison of BD Kiestra TLA combined with MALDI-TOF-MS versus conventional methods.	Clinical blood cultures.	TAT to growth detection. TAT to identification. Possible clinical impact to antibiotic prescription.	- Kiestra TLA combined with MS resulted in 30.6 h time gain for isolate identification in compared to conventional methods. - Early microbial identification without susceptibility testing led to an adjustment of antibiotic regimen in 12% (24/200) of patients.
Froment et al. (16)	Prospective comparison of fully automated InoqulA (BD Kiestra) vs manual method.	Calibrated bacterial suspensions and clinical specimens (urine or swabs).	Recovery of bacterial strains. Quality of colony separation. Reproducibility. Total time for inoculation and streaking.	- Higher quality of isolation with automated method ($P = 0.0006$ and $P = 0.0002$ for mono- and polymicrobial plates respectively). - No difference in streaking rate and inoculation time.
Mischuk et al. (18)	Prospective comparison of manual	Wound swabs samples.	Quality of isolation.	More often individually distinct and
Continued				

Reference	Type of study	Type of sample	Studied outcome	Summary of main results
	versus automated plating with Previ Isola system.			less confluent colonies with Previ Isola than with manual method.
Jones et al. (18)	Prospective comparison of automated culture of <i>Staphylococcus aureus</i> from flocked swabs versus that of manual culture of fiber swabs.	Nasal swabs.	Diagnostic performances (sensitivity).	Automated culture significantly increased the detection rate by 13.1% for direct culture and 10.2% for enrichment culture.

TAT, turnaround time; LIS, laboratory information system.
*Start time for TAT calculation was considered the time of specimen accessioning and bullet of the test.

microorganisms to room temperature and atmospheric oxygen (3).

INCREASED LABORATORY EFFICIENCY

TLA is critical in a landscape of ever-increasing microbiology test volume while laboratories must contend with personnel shortages and economic restrictions. Many studies performed over the past several years advocate for the optimization of laboratory workflow leading to improved productivity and decreased processing TAT (28, 34–40). Given that manual inoculation and transferring of plates between benchtops and incubators occupy approximately 33% and 10% of a technologist’s time, respectively (3, 41), there is a great potential of improvement due to an automated system. Compared to manual streaking, a few studies have demonstrated that automated inoculation exhibits a significant decrease in hands-on-plating time (14, 26, 27, 30). A 2018 study (42) evaluated the sample processing time (preparation and streaking time) of manual method versus automated streaking with the Previ Isola system in blood and urine clinical specimens. While there was a high consistency of bacterial growth between the 2 methods and a high concordance in terms of quantity of colony counts, the Previ Isola demonstrated lower hands-on-time for inoculation per sample. The authors calculated that they could save about 6 min of hands-on-time of a skilled technologist per 10 samples. While these savings may appear to be minimal, when extrapolated it showed that 1.25 8-h work days are saved per 1000 cultures. This efficiency gain can be substantial in the face of labor shortages and increased demands on the laboratory.

In addition to reduction in hands-on-time, TLA offers the additional advantage of reduced processing time for almost all the processing steps of a bacterial culture (28, 34–40). Compared to manual plating, in which a technologist may inoculate several specimens before transferring plates to an incubator, the so-called “smart” incubators of automated systems eliminate plates waiting in the setup area and allow direct incubation after inoculation. These incubators maintain consistent temperature and gas levels with negligible heat and CO₂ gas loss enabling the first plate images for culture interpretation to be ready as early as after 10 h for urine specimens and 8 h for positive blood culture broth subcultures (1, 11, 34, 35, 43). Digital plate imaging can facilitate scanning for growth more frequently or even continuously (depending on the laboratory’s workflow) instead of only at set times during the day. Laboratories may consider that reducing time of reporting microbial growth may result in a reduction of sensitivity (37). Additionally, if a laboratory chooses to reduce the incubation time, it should also consider the need to validate additional ancillary testing performed at earlier timepoint than previously performed in the laboratory, such as identification, susceptibility methods, and biochemical tests.

IMPACT ON PATIENT CARE

While the positive impact of TLA on the laboratory workflow has been shown in numerous studies, most of these studies have evaluated the impact of TLA on the laboratory workflow. Recent studies have demonstrated statistically significant reduction in time to final report (from 71.6 h to 61 h for positive urine specimens, from

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52.1 h to 28.3 h for sterile urine specimens and from 55.4 h to 32.8 h for positive blood cultures, $P < 0.001$) (35, 37, 39, 40) with automated systems. Combination of the improved efficiencies gained by use of a TLA system with rapid identification methods such as MALDI-TOF-MS for bacterial identification can further enhance the reduction of reporting time. One study (36) compared the time to identification on positive blood cultures of conventional methods versus BD Kiestra TLA combined with MALDI-TOF-MS, observing a gain of 30.6 h for isolate identification with automation.

Whereas most of the studies describe reduced reporting times with laboratory automation, a few studies have demonstrated the opposite results that might be observed as well. In a comparison of the time to final identification during 2 study periods (pre- and post-installation of Inoqula BD Kiestra) for urine specimens (28), the authors reported that, while a significantly shorter time to identification during the automation period was noted for sterile cultures, a slightly higher time was observed for positive cultures when 2 species were identified. A separate study also reported significant increased time from receipt to inoculation (23 min vs 32 min) and total processing time (from 28 min to 66 min) postautomation using the BD Kiestra TLA system and a similar study design as previously noted (38). There was, on the other hand, a slight decrease in time to final report (from 43.8 h to 42 h) attributed mainly to the decrease in TAT of negative results. The authors of this study argued that the workflow for these specimens included a batching step in which specimens were saved in a tabletop rack before being loaded on the TLA instrument. The delay encountered in the post-TLA period accounted for the time the specimen was on the counter waiting to be loaded, or on the instrument waiting to be plated rather than in active hands-on time. Those surprising findings suggest that although there is a great potential for decreasing the time to reporting results using automation, TLA implementation does not automatically eliminate human or hardware bottlenecks or inefficient processes. To harness the maximum impact of TLA, clinical microbiology laboratories might need to adopt changes in laboratory workflow through the entire process from specimen reception, inoculation, incubation, and imaging whereby culture work-up can begin as soon as cultures are ready to be read.

Large-scale studies have not yet been performed to demonstrate a significant impact on clinical outcomes.

To our knowledge, only 2 studies have tried to evaluate the potential impact of TLA on patient care. One study (36) assessed the possible clinical impact of microbial identification results using TLA and MALDI-TOF according to antibiotic treatment prescription decision timepoints. For 33.5% (67/200) patients, there was no impact on antimicrobial treatment based on the

identification. Antimicrobial treatment, however, was modified following the Gram stain result (14.2%), initial identification (12%), and identification and susceptibility result (34.5). These results demonstrate that a significant number of prescribing decisions are made based on the results generated by the laboratory and optimization of those results may influence more timely clinical decisions. A second study retrospectively compared 8 h of incubation and digital plate imaging with BD Kiestra Work Cell Automation versus an overnight incubation period (35), reporting a significant reduction on duration of empirical therapy (86.9 h vs 54.8 h, $P < 0.001$), although no differences were observed regarding the proportion of patients receiving de-escalation or escalation therapy after microbiological report. The crude all-cause death rate was significantly lower ($P = 0.037$) during the automation period. Nevertheless, authors did not provide data regarding appropriateness of antibiotic therapy for both groups and it seems difficult to assign this effect solely on the impact of automation. Additional studies assessing the impact of reduced turnaround time and standardization of culture reading on clinical outcomes are needed.

INCREASED WORKPLACE SAFETY

Worker safety is one of the most important advantages of automating industrial operations. Technologists do not have to handle most specimens with automated processing. Since the steps of transferring culture plates to incubators, examination of cultures with digital imaging, automation of identification and antimicrobial susceptibility testing, and handling of culture plates by technologists has been limited to the bare minimum, consequently the exposure risk to potential pathogens is minimized (11, 12, 25).

Decreased long-term costs. The laboratory budget is a primary determinant of organization and management and thus one of the main drivers and barriers of laboratory automation implementation. Implementation of TLA represents an important investment, which is inevitably associated with a short-term escalation of cost for accommodating the project (12). In a real-world evaluation of integrating an automated instrument for diagnostic microbiology within a model of TLA (25), the period of payback for integration of WASPLab in a model of TLA was estimated to be 7.3 years. The overall savings could be estimated from lower personnel costs, from saving of disposables and manual tools and from the elimination of 1 (standalone) incubator. One group of investigators demonstrated that they were able to reduce staffing for both processing and working up specimens, decrease time to results and costs by performing fewer subcultures or earlier reading of cultures and increase the number of specimens processed (11). In their model, they were able to pay back the investment in

3 years rather than their projected 5 years through labor savings alone (11). In a separate evaluation of the financial impact of TLA at 4 facilities, there was an increase in total staff productivity (specimens per full-time employee) ranging from 18% to 92% following implementation. Among these facilities, annual savings per year ranged from \$270 000 to \$1 200 000 (44). These several studies point to the fact that the question should not be whether the laboratory can afford the investment in TLA, but rather whether the laboratory can afford not to invest in TLA given the labor shortages laboratories face.

Challenges for Automation Implementation

Despite the many advantages in efficiency, productivity, and timeliness that automation offers, it is not without new and unique challenges. For every advantage that laboratory automation provides, there are similar challenges that a laboratory must face. The laboratory must determine what is feasible within their current system and constraints. Properly approached, there are a number of important benefits that can be achieved through implementation of automation in the clinical microbiology laboratory. Successful implementation, however, can be a major barrier to realizing the advantages for automation systems. Before selection of an automation system, laboratories should identify requirements criteria to determine the automation system that should be selected. Items such as space, performance, analytical criteria, maintenance, and cost should all be thoughtfully considered before selection of an automation system (Table 2).

Laboratories should also consider and agree on the expectations they have for the impact of the automation system on the laboratory. Studies of automation of core laboratory systems (i.e., chemistry, hematology, and coagulation) have demonstrated an 86% reduction in manual processing steps (45). However, automation of the microbiology laboratory still requires many manual steps of culture interpretation, work-up, and identification and susceptibility testing, until these processes become automated in the future.

CONNECTIVITY

The introduction of automation in diagnostic bacteriology is aimed at improving laboratories' productivity, quality, and traceability, but its integration in routine diagnostic laboratories is challenging. Among other difficulties, the successful interface of the system with laboratory information systems (LIS) and with other automates is complex and crucial to guarantee a successful achievement of the laboratory objectives and expectations.

The connection of the systems with the LIS is mostly unique for each laboratory since multiple different LIS are commercialized. Even laboratories using the same LIS often have different settings based on their different workflows, activities, and organization. Moreover, automated system management software and application functionalities may not be compatible with all LIS and/or with the different laboratories' workflows. It is thus strongly recommended to thoroughly determine the compatibility of each software or imaging application with the LIS specifications before moving to acquisition of the systems. Due to the relative novelty of laboratory automation in diagnostic bacteriology, technologists do not have an extensive overall expertise in automated systems, LIS, information technology (IT) specifications, and strict IT security settings. Thus, it is essential to involve expert stakeholders from both automated systems manufactures and the laboratory IT and LIS to design the complex interface of the automated systems with the LIS. A continuous collaborative work between these experts during the entire project is absolutely required to quickly solve any major issues that will be faced during the installation and implementation processes. Ideally, each manufacturer should offer an interface-testing environment to test the system management software's connectivity and functionalities with the LIS and IT before the installation of the automated systems. Preinstallation interface testing represents a very interesting possibility to solve most issues ahead of the installation and accelerate the postinstallation go-live of the system.

It is also important to consider that any upgrade or modification of the system management software, computer operating systems, and the laboratory IT or LIS may create functional issues and failure of the bidirectional interface. Thus, any minor or major upgrade require attention and should be considered as a new project with potentially additional significant human and financial investments to ensure continuous and scalable functionalities of systems.

FINANCIAL CONSIDERATIONS

Despite the previously mentioned financial benefits of TLA, the significant initial investment may be a barrier for some laboratories, along with difficulty in performing their own projections for financial justification of the investment. There are several strategies laboratories may use to determine how they will justify the return on investment and payback period for TLA systems (25). Each laboratory must perform an analysis of their local systems to determine what may be expected with implementation of a TLA system (Table 2). Ultimately, each laboratory must determine what is considered a measure of success for implementation of the system.

CHANGE IN LABORATORY ORGANIZATION AND STRUCTURE

Changes in workflow and staffing will lead to a requirement for gaining staff support and buy-in for implementation. Change management strategies should be used to lead to a successful implementation and support among the technical staff. Ultimately, all of the changes that will be experienced with automation in the clinical laboratory must be managed through effective leadership. There are 2 very different ways to approach change management within systems: motivation through penalties and rewards or creating an environment that encourages and maximizes internal motivation (46). The laboratory setting is no different. Much of the work that is conducted in the laboratory is based on the former, which establishes a transactional relationship based on regulatory requirements and quality control standards that pass or fail. There is, however, opportunity to use implementation of automation to create a transformative environment where staff gain more connection to their work and are valued as members of the transformation in the laboratory. Effective leadership strategies that engage staff from the beginning of the implementation of an automation system and throughout the ongoing quality control and monitoring is critical to ongoing and continued improvements in the laboratory.

Future Directions

As previously discussed, automation has brought substantial changes in clinical microbiology laboratory organization and has modernized the diagnostic approach to a clinical sample. What does the future hold for clinical microbiology remains yet to be seen. The near future of laboratory automation will most likely be affected by the spread of automated image reading expert systems and algorithms with multiple added-value applications. Those new technologies will allow earlier detection of microbial growth, automated detection, and autorelease of sterile samples, identification and quantification of bacterial colonies, or even automated reading of antibiotic susceptibility testing disk diffusion assays and thus further decrease TATs and increase productivity (13). Further, integration of additional patient demographic information that impact the culture interpretation (i.e., age, gender, other laboratory values, and previous cultures) can be gathered from the LIS to aid in automated advanced interpretation of cultures. One could consider that expert systems are the realization of a more complete automation from sample to final results with minimal human intervention during the diagnostic process.

Future efforts in the field of automation should also focus on impacting the patient management and from this point of view efficient communication of a microbiological result to clinicians is crucial. Shorter TAT for final results of microbiological samples do not

automatically result a clinical decision for the patient. Communication barriers between the microbiology laboratories and clinical units due to verbal reporting of test results, information transfer between poorly integrated IT systems, limited advisory/consult services or restricted “opening hours” must be overcome (47). A computer-based communication of results (with an alert system for critical results for example), together with a reorganization in management of laboratory workflow and clinical staff may serve as a valuable framework to establish these changes and allow around the clock reporting of microbiological results coupled with a faster clinical decision aiming to improve patient’s care.

Although it has taken 30 years since the first automation systems were introduced in the microbiology laboratory, TLA is now a recognized and valuable component of the laboratory. As with all new advances, there continues to be need for further optimization and improvement in the hardware and software as laboratories gain experience and needs continue to expand. It is clear, however, that with TLA we are currently experiencing a fundamental change in the composition of the clinical microbiology laboratory. However, despite the automation of most specimens for culture processing, there will likely always be unusual specimens that will be unable to be processed on the TLA system. Similarly, while there have been many advances in image analysis and artificial intelligence, there will always be a need for clinical microbiology expertise to interpret the complex information, emerging microorganisms, and variety of resistance patterns presented in clinical microbiology. Experienced technologists will always be needed to augment the use of TLA. Although the present and the future of clinical microbiology is increasingly automated, there will always be a need for highly qualified technologists working collaboratively with the automated system to complete the work of the microbiology laboratory.

Nonstandard Abbreviations: TLA, total laboratory automation; LIS, laboratory information systems; IT, information technology.

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