Reduced turnaround time for blood culture:
Experiences from an improvement process

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Abstract

Background
Customer satisfaction is important for clinical microbiology laboratories and the most important service aspect is the reliability of responses. One important indicator of the quality of care is turnaround time for a sample referred to a laboratory.

Aim
This study describes and evaluates an improvement of the blood culture process and evaluates the staff’s experiences of the changes brought by the improvement project.

Methods
The blood culture process during evenings and nights was re-designed in a cooperation project between the laboratories of clinical microbiology and clinical chemistry in a mid-size Swedish county council. Typing with matrix-assisted laser desorption/ionization time of flight (MALDI ToF) and rapid antibiotic susceptibility testing were also introduced. To describe staff experiences semi-structured interviews were performed with twelve of the staff involved.

Results
The time from sampling to susceptibility testing and typing, for patients with cefotaxime resistant enterobacteriaceae, was before the improvement project on average 55 hours compared to 43 hours after closure of the project. In the qualitative content analysis four categories were found which represented the experience of the staff: patient focus, changed knowledge, cooperation and driving forces.

Discussion
The study of the implementation of the improvement showed that laboratory staff could handle the change well. The change from traditional biochemical typing, used for over 50 years, to MALDI ToF is indeed a paradigm shift. Nevertheless, nobody was disappointed over the fact that some of the fundamental previous microbiological laboratory work routines were laid to rest.

Keywords: Quality improvement, clinical microsystem, MALDI ToF, Rapid susceptibility testing, turnaround time
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Introduction

Background knowledge

Various methods have been developed for continuous improvement of work processes. Three examples are the Toyota Production System (Thompson 2003) which later evolved into Lean, Six Sigma (Schweikhart et al. 2009) and the concept of "clinical microsystems" (Nelsen et al. 2002). Clinical microsystems are defined as "a small group of people who work together on a regular basis to provide care to discrete subpopulations of patients" (Nelsen et al. 2002, p. 474).

Customer satisfaction is an important factor in improvement of clinical microbiology laboratories. The most important service aspect is the reliability of responses. One important indicator of the quality of care is turnaround time (TAT) for a sample referred to a laboratory (Howanitz 2005). TAT often measures the time from sample registration to the reporting of results. In clinical microbiology laboratories in Sweden, one of the “medical quality indicators” (MQI) is the time from sampling to the incubation of a blood culture. A blood culture should quickly be incubated in the right environment (36.5 °C).

Infections of the bloodstream are associated with significant morbidity and mortality. Rapid administration of appropriate antibiotic treatment is crucial to increase survival (Leibovici et al. 1998, Lodise et al. 2003). To achieve this, it is important to ensure the correct identification of microorganisms. The recently introduced mass spectrometry, matrix-assisted laser desorption/ionization time of flight (MALDI ToF), is a rapid and accurate typing method for bacteria and yeasts (Ferroni et al. 2010, Prod’hom et al. 2010, Stevenson et al. 2010), and may therefore reduce TAT.

The results of rapid antibiotic susceptibility testing (RAST) performed directly on samples from blood culture bottles has been compared to conventional susceptibility testing performed on colonies after subculture, with acceptable results for Gram-negative rods (Ling et al., 2003, Chen et al., 2008), whereas for Gram-positive bacteria conflicting results are reported (de Cueto et al. 2004, Ling et al. 2003, Coyle et al. 1984).

In a debate article entitled “Archaeological laboratory results or microbiology in time?” three physicians at three different clinical microbiology laboratories highlights the problem of response times (Sundqvist et al. 2011). Despite the rapid development of molecular biology, antigen testing and rapid species identification and susceptibility testing of bacteria, clinical microbiology laboratories suffer from slow methods and lack of logistics (Sundqvist et al. 2011). Many microbiological laboratories in Sweden are currently working to improve processes and introduce new technologies.

![Diagram](image)

Figure 1. The process of blood culture.
Local problem

Behind every blood culture is a long chain of events (see figure 1). The process starts with sampling of the blood, primarily performed at the ward where the patient is treated. The time from sampling to proper incubation of blood culture bottles is a good assessment of logistic routines. When measuring the MQI for blood cultures at 14 laboratories in Sweden in 2009, it was found that around 48% of the bottles arrived to the laboratory on the day of sampling, 49% on the next day and more than two days were required for 3% (Swedish society for microbiology, 2009). Transportation time should, according to the supplier of the blood culture system, be as short as possible and not exceed 24 hours. In 2006 the first improvement was performed in Jönköping when staff at the clinical chemistry laboratory was trained to incubate the blood culture bottles once every night (at 01 AM). The laboratory situated at the county hospital Ryhov in Jönköping receives samples from two other hospitals: the Highland hospital in Eksjö and the Värnamo hospital. Transportation times in the county of Jönköping have been measured annually since 2006. When the measurement started, the longest transportation time occurred due to the lack of daily transports from the remote hospitals on Sundays. This was improved in 2010 when transports on weekends were introduced.

Recently several improvements of the blood culture process have been performed in the county council of Jönköping. Rapid tests directly from blood cultures were introduced (coagulase for Staphylococcus aureus and chromagenic culture media for enterobacteriaceae), and 20% of the bacteria could be typed the same day. The introduction of MALDI ToF will further improve the response time. In studies typing with Maldi ToF on bacterial strains, 95% could be typed to the genus level (Cherkaoui et al. 2010, Mellmann et al. 2008, van Veen et al. 2010). Directly from the blood culture, without subculture, 79% could be typed (Prod’hom et al. 2010). Another method is to subculture for two hours after the indication of growth in a blood culture bottle. By this method, 98% were then successfully typed by MALDI ToF (Kroumova et al. 2011).

The change from traditional biochemical typing methods, used for over 50 years in the laboratory, to MALDI ToF is a paradigm shift. This may be perceived differently by different employees. The, somewhat tacit, knowledge built up during years of working experience will suddenly be replaced by an instrument. Presumably, employees will experience a mixture of delight to experience such a revolution and sorrow that one of the most fundamental microbiological work routines is laid to rest.

Intended improvement

The aim of the quality improvement project was to enhance the blood culture process. The first part of the process to improve was the flow of blood cultures taken on evenings and nights. Together with the staff at the clinical chemistry laboratory the handling of blood culture samples was optimized. The next intervention was to validate RAST and introduce this as a routine method. The last intervention was to validate and introduce a new typing method, MALDI ToF. Furthermore, to improve the pre- and post-analytic phases, collaboration with two clinics, the emergency clinic and the infection clinic, was performed. To recognize when an adequate treatment was introduced, for patients with cefotaxime indeterminate or resistant (CTX: I and R) enterobacteriaceae journal reviews were performed.
Study questions

There were two study questions: 1) How might the blood culture process be improved, with decreased TAT, to make faster adequate treatment of the patient possible? 2) What are the perceived staff experiences of the changes performed to improve the blood culture process?

Methodology

Ethical issues

Journal reviews are necessary to examine the time to adequate treatment. Improving health care is regulated by healthcare legislation and to subsequently record, check and study when and with which antibiotics the patient is treated, is not considered as an ethical risk to the patient.

Interviews were performed with six persons employed at the clinical microbiology laboratory who worked with blood cultures as well as with six of the persons employed at the clinical chemistry laboratory. Each interviewee had the opportunity to give consent to the interview or deny participation. The interviewees were given written and verbal information about the study. All participation was voluntary and could be canceled at any time without consequences for the interviewees. If quotations were used, the interviewees were informed and gave their consent. An ethical review of the study was performed through the Health Sciences Ethics Review Board (The School of Health Science, Jönköping University, Sweden) no 12-4.

Setting

The Department of Laboratory Services is part of the Division of Medical Services, which is a self-governing unit within the Jönköping County Council. Activities include ten units distributed among the county’s three hospitals and health care centers, performing approximately 3.7 million tests annually. Among the 330 employees there are biomedical technologists, nurses, physicians, healthcare administrators and engineers. The Clinical microbiology laboratory in Jönköping serves three hospitals in the county. Sample transports are carried out by the County Council transport service. During weekdays five cars transport samples from the primary healthcare centers and hospitals to Ryhov. On weekends there is one transport from the remote hospitals. Half of all blood cultures are from the two county district hospitals. The number of blood cultures has increased from 5775 to 18711 from 1994 through 2011 (figure 2).

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of blood cultures</th>
</tr>
</thead>
<tbody>
<tr>
<td>1994</td>
<td>5775</td>
</tr>
<tr>
<td>1995</td>
<td>6285</td>
</tr>
<tr>
<td>1996</td>
<td>6832</td>
</tr>
<tr>
<td>1997</td>
<td>7313</td>
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<tr>
<td>1998</td>
<td>7791</td>
</tr>
<tr>
<td>1999</td>
<td>8280</td>
</tr>
<tr>
<td>2000</td>
<td>8742</td>
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<tr>
<td>2001</td>
<td>9201</td>
</tr>
<tr>
<td>2002</td>
<td>9657</td>
</tr>
<tr>
<td>2003</td>
<td>10113</td>
</tr>
<tr>
<td>2004</td>
<td>10575</td>
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<tr>
<td>2005</td>
<td>11034</td>
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<td>2006</td>
<td>11492</td>
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<td>11945</td>
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<tr>
<td>2008</td>
<td>12397</td>
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<tr>
<td>2009</td>
<td>12846</td>
</tr>
<tr>
<td>2010</td>
<td>13291</td>
</tr>
<tr>
<td>2011</td>
<td>13737</td>
</tr>
</tbody>
</table>

Figure 2 Number of blood cultures processed at the clinical microbiology laboratory, Jönköping 1994-2011.
Jönköping County Council has a long tradition of process improvement in clinical microsystems and the Division of Medical Service in Jönköping has since 2007 worked with improvement in this context. New employees are trained to work with the microsystem model. The number of improved processes is reported yearly in the balanced score card. In 2009 the number of improved processes was 58, in 2010 it was 104, and in 2011, 150. Deviation reporting (264 deviations were reported in 2011) is another important clinical improvement tool at the department of clinical microbiology in Jönköping and many of the deviations provide the foundation for clinical microsystems.

**Planning the intervention**

In March 2011, a process to improve the flow of blood cultures in evenings and nights was designed, together with the unit of clinical chemistry. Staff was trained by the specialist responsible for the blood culture process. During two weeks in September and October 2011, time from sampling (time when the computer order was send to the laboratory) to incubation for 725 blood culture bottles, was measured. Samples with paper referrals where the sampling time was not specified were excluded from the study. This quantity was the annual MQI conducted at multiple clinical microbiology laboratories in Sweden (Swedish society for microbiology, 2009).

In the autumn of 2011, RAST was validated. Briefly, five drops from the blood culture bottle mixed with 1,5 ml 0,9% sodium chloride and spread on a Müller Hinton plate with 5% horseblood and antibiotic discs containing cefotaxime, ceftazidime, ciprofloxacin, tobramycin, piperacillin/tazobactam or meropenem were placed on the plate which was incubated in 37 ºC in air with 5% CO₂ for 6 h and then the diameter of inhibited growths around the discs were measured. Each bacterium was then classified as sensitive (S) or resistant (R) to respective antibiotic. The validation was made using 50 consecutive enterobacteriaceae isolates For each of the six antibiotics, histograms of measured zone diameters were compared with histograms produced using the reference method. The reliability of limits established between S, I or R, was evaluated for each individual antibiotic. In December 2011 the RAST method was introduced.

In October 2011, typing of bacteria by MALDI ToF was validated by comparing the result with the results of traditional typing. Thirty-nine reference strains from CCUG (Culture Collection, University of Göteborg, Sweden) and ATCC (American Type Culture Collection) and 62 external quality control strains from United Kingdom National External Quality Assessment Service (UK NEQAS) for Microbiology, was used. The change from traditional typing to MALDI ToF was discussed several times by the staff. Procedures for how to change work routines were for example discussed at two workshops in December 2011.

**Planning the study of the intervention**

How can the blood culture process be improved, with decreased TAT, to make faster adequate treatment of the patient possible? For patients with cefotaxime indeterminate or resistant (CTX: R) enterobacteriaceae in the blood culture, without adequate treatment when blood culture was positive, the number of days from sampling until the patient received adequate treatment was measured before and after intervention.

To determine how the staff perceived the changes brought by the improvement process, semi-structured interviews were performed with six of the staff working with blood cultures in the clinical microbiology laboratory, and six members of the staff at the clinical chemistry laboratory, who incubate blood cultures. This was a qualitative measurement of how staff perceived change.
The questions were based on the quality improvement framework 5 P’s (Nelson et al. 2002) Purpose, Patients, People, Process and Pattern with the addition of a 6th P Passion (see the interview guide in appendix 1). An analysis of the interviews was made by qualitative content analysis and the interviewees’ responses were condensed to categories and codes. The codes will represent the experience of the staff.

**Methods of evaluation**

For each of the three hospitals in the region, mean times from sampling to incubation for all blood culture samples during two weeks in the autumn was followed from 2006 until 2011. Comparison with 21 laboratories in Sweden in the MQI measurements was also done. A detailed analysis was also performed at the County Hospital Ryhov regarding cultures taken evenings and nights, and compared with figures from the previous year. This was done using control charts. The measurements also covered periods when staff at the clinical microbiology laboratory had left for the day, on weekdays after 6 PM.

An evaluation was performed after that the first 15 strains were processed after the introduction of RAST to further validate this work process. A further validation of the MALDI ToF typing results was performed during two days when strains from blood cultures and urine samples were typed, and compared with the results of conventional typing.

To determine the clinical perspective, 27 patients with CTX: R enterobacteriaceae in the blood culture were selected during 2011 and the spring 2012. Patient with and without adequate treatment were registered by journal reviews. The mean time from sampling to susceptibility testing for the 27 patient was compared before and after improvement with RAST. The time from positive blood culture to susceptibility testing was also measured. For patients with CTX: R enterobacteriaceae in the blood culture, without adequate treatment when blood culture was positive, the number of days from sampling until the patient received adequate treatment was measured.

Boyle et al. (2012) used semi-structured interview of 55 pharmacists to analyze introduction of quality improvement programs and focused on staff attitudes to quality-related event reporting. In a study performed to describe the experiences of nurses to a recently implemented quality register eight nurses were interviewed (Rosengren et al. 2012). In semi-structured interviews an interview guide with themes is typically followed, but the interviewee also had the possibility comment in free text (Hartman 2004). In a semi-structured interview there are themes of tasks to complete, but it also wants to give fairly wide margin of possible unfolding and deepening (Alvesson 2011). The interview guide was inspired by the questions of the quality improvement framework 5P’s (Nelson et al. 2002) Purpose, Patients, People, Process and Pattern with the addition of a 6th P for Passion (see the interview guide in appendix). “5P” is often used to analyze how a clinical microsystem works. The questions were modified by the author to focus the change of the blood culture process: The intervention to improve the flow of blood cultures in evenings and nights, the typing with MALDI ToF and the RAST. The interview guide was tested and revised by one of the employee at the clinical microbiology laboratory and then it was adjusted to the final version.

In the study all twelve informants were interviewed face-to-face. Interviews lasted in average 20 minutes. The interviews were audio-recorded and then transcribed verbatim. All the questions were open questions and some questions had to be clarified. The data collection focused on staff experiences of implementing and working with the improvements.
Analysis

Time from positive blood culture to the response of susceptibility testing was calculated for 27 blood cultures with CTX: R enterobacteriaceae. To understand how rapid the process could be the minimum time was calculated. To analyze how great the problem with patients without adequate treatment was, the number was counted for 2011. For the 13 patients without adequate treatment during the test period the time from sampling to adequate treatment was analyzed. Analysis was performed if however a telephone message from the physician at the clinical microbiology laboratory to the staff at the clinic resulted in a change in antibiotic treatment.

The interviews were read through several times. Meaning units that contained information relevant to the issues of the study were selected. From the meaning units codes were identified, and combined to categories. Quotes illustrating each category were taken from the interviews (Lundman & Granheim 2008). Analysis of the interviews was made by qualitative content analysis (Lundman & Granheim 2008). For example: “Today, it is watertight bulkheads between the departments and also in the leadership” was condensed to “We didn’t work together” and the code was “Barriers for cooperation” in the category “Cooperation”. “New employees would lack basic way of thinking in bacteriology” was condensed to “new employees will lack knowledge” and the code was “Tacit knowledge will be forgotten” in the category “Changed knowledge” (see the analysis in appendix 2). The codes were identified and grouped into four categories (e.g. Patient focus, changed knowledge, cooperation and driving forces).

Results

Outcomes: Nature of setting and improvement intervention

The management of the Division of Medical Services had since the laboratories for clinical chemistry and clinical microbiology was located together in 2005 worked to increase the possibility of collaboration. When the improvement project for blood cultures sampled at evenings and nights was presented and the staff training began, one of the employees asked after the training: "I work tonight, can I start right now?" This shows how enthusiastic one of the staff was towards the improvement.

The management had in recent years focused on a reduction of TAT. The staff at the clinical microbiology laboratory had since 2007 worked in clinical Microsystems and two main foci had been formulated, RAST and bacterial typing with MALDI ToF. The change from traditional typing to MALDI ToF was discussed several times by the staff. Procedures for how to implement the new routines were discussed at two workshops in December 2011. Two different solutions were discussed by the staff and the conclusive solution was introduced. The improvement intervention process is presented in figure 3.
Clinical microsystem focuses on the work processes, and when problems arise the group will try to find solutions and cooperate to improve routines. One lesson learned from the process of improvement is that one improvement in a certain part of the process often changes some other part of the process. For example, when typing with MALDI ToF and RAST were introduced, more work had to be done in the afternoon and staff resources had to be rescheduled. Some of the staff felt a bit strained when the RAST was introduced but now all are positive.

In the qualitative content analysis four categories were found which represent the experiences of the staff. Both the uniqueness and variation within the different views are described and exemplified with quotations.

The first category was patient focus. The codes were: faster responses and more correct responses. All interviewees were aware that the focus was to obtain a faster and more correct response for the patient. The staff expectations were that patient safety would increase using MALDI ToF as a tool for typing. One of the interviewees of the clinical chemistry staff said that the purpose was to assist staff in clinical microbiology laboratory, while the remainder said that the intention of the change was a faster response.

The second category was altered knowledge. The code were: tacit knowledge will be forgotten and less opportunities for verifying. Regarding the tacit knowledge required by manual typing, staff believed that “new employees would lack basic way of thinking in bacteriology”. Hopefully the old knowledge would not be forgotten. The implementation of MALDI ToF would also change other processes. One disadvantage perceived by staff was less opportunities to verify the bacterial species compared with the previous typing methods. The staff would not miss the biochemical tests, but felt great relief in the change to typing using MALDI ToF.

The third category was cooperation. The codes were: cooperation in the blood culture process and barriers for cooperation. The cooperation in the blood culture process works very well. The change process was not perceived as particularly difficult and blood cultures were taken care of at least every two hours. The cooperation between clinical chemistry laboratory and clinical micro-
biology laboratory were before this work limited. Different computer systems and facilities were seen as obstacles to cooperation by the interviewees “We share today only instruments; we will not analyze each other sample”. One of the clinical chemistry employees said that one barrier for cooperation was the leadership: “Today, it is watertight bulkheads between the departments and also in the leadership”. Suggestions for improvement that emerged were to place the blood culture machine.

The last category was the driving forces. The codes were to develop, to learn more and to obtain better outcomes. All the interviewees performed well. Some of the driving forces for the change on behalf of the staff were to develop, learn, and obtain better outcomes, such as safer and faster results. Motivators were responsibility for learning new methods.

**Outcomes: Changes in processes and patient outcomes associated with the intervention**

In 2011, 21 laboratories took part in the national MQI measurement. 58% of blood culture samples were received in the laboratory on the day of sampling and 40% the following day and more than two days were required for 2%. In the county of Jönköping 66% of blood cultures were received on the day of sampling and 34% the following day and for no blood cultures more than two days were needed (Table 1.).

Table 1. Numbers of blood cultures incubated at the day of sampling, the, next or more than two days after sampling. (*Personal communication.)

<table>
<thead>
<tr>
<th>No. of Laboratories</th>
<th>The same day</th>
<th>+ 1</th>
<th>≥ 2</th>
<th>No. of blood cultures</th>
</tr>
</thead>
<tbody>
<tr>
<td>21 clinical microbiology laboratories in Sweden *</td>
<td>58%</td>
<td>40%</td>
<td>2%</td>
<td>17220</td>
</tr>
<tr>
<td>Clinical microbiology laboratory Jönköping</td>
<td>66%</td>
<td>34%</td>
<td>0%</td>
<td>725</td>
</tr>
</tbody>
</table>

The mean time from sampling to incubation for blood cultures, from the three hospitals in the region, was measured during two autumn weeks in 2006 through 2011. For all three hospitals a marked reduction of the time is noted from 2008 until 2011 (Figure 4).

![Figure 4. Mean time from sampling to incubation for blood cultures during two weeks in the autumn for the three hospitals in the region 2006 through 2011.](image-url)
A detailed analysis, using control charts, was performed for the County Hospital Ryhov, regarding cultures taken evenings and nights. The measurements were made before and after intervention (2010 and 2011) at a Thursday and covered periods when staff at the clinical microbiology laboratory had left for the day (after 6 PM). Before the intervention, a shift from about two hours to six hours was noted for the time from sampling to incubation for blood cultures received when the microbiology-staff had left for the day. This shift could not be observed in 2011, after the intervention (Figure 5).

Figure 5. Time (hours) from sampling to incubation of blood cultures illustrating a weekday process at Ryhov 2010 and 2011.

A initial validation of RAST was done by comparing results from conventional susceptibility testing. Fifty strains of enterobacteriaceae were used in the validation. 35 strains were classified as S to all antibiotics by both methods but 15 strains were R to one or more antibiotics in the RAST. Five of these were repeatedly R, four were I and six S, using the conventional method (one example figure 6). One strain was changed from S to I. The RAST is thus only valid for classification of a bacterium as S and R for an antibiotic, and is designed to prevent any R isolate to be incorrectly reported as S. This is to avoid the risk that a patient may get inadequate treatment.

Figure 6. Ciprofloxacin diameter (mm) for 50 enterobacteriaceae tested with rapid susceptibility testing. <19 mm is resistant and ≥19 mm is sensitive. In conventional susceptibility testing two of the resistant strains were repeatedly resistant, one strain was indeterminate and one strain became sensitive.
Further validation of RAST was then performed on 15 consecutive isolates: nine were S to all antibiotic and six isolates were R to an antibiotic in the RAST. Four of the R strains were confirmed as R, one was I and one S using the conventional methods.

Thirty-six out of 39 (92%) reference strains and 44 out of 62 (71%) external quality control strains from UK NEQAS, were correctly typed using MALDI ToF. Bacterial strains sent to the clinical microbiology laboratory from UK NEQAS represent types rarely isolated and known to be difficult to type. Discrepancies were found for Shigella and Streptococcus pneumoniae, thus the conventional typing methods was retained for these species.

Thirteen of 27 patients (patient in 2011 until April 2012) with CTX: R enterobacteriaceae in the blood did not receive adequate treatment at the time of a positive blood culture. Time from sampling to susceptibility testing and typing was measured. Before the implementation of RAST, it took in average 55 hours versus 43 hours after implementation. The minimum time was 24 hours and 18 minutes. The mean time from a positive blood culture to the report of susceptibility testing was 25 and 6 hours before and after improvement, respectively. Before the implementation of RAST, it took between one and seven days from the time of sampling until the patient received appropriate treatment. For nine patients there is documentation that the doctor at the laboratory called the clinic and reported the finding and the same day the antibiotic treatment was changed to adequate therapy. The mean time from sampling to adequate treatment was three days. There was only one patient discovered without adequate treatment after the RAST was introduced. This patient received adequate treatment within two days.

A discussion with the staff at the emergency department regarding the pre-analytical phase was performed. They were aware of that blood cultures immediately should be sent to the clinical microbiology laboratory but sometimes a lack of transportation is observed. Now the staff will improve the pre-analytical phase. For the post-analytic phase a discussion with physicians at the department of infectious diseases was performed and the focus was RAST and bacterial typing with MALDI ToF and how the clinical perspective may be improved with lower TAT for blood cultures.

**Discussion**

**Summary**

In this quality improvement project the focus was on the patient. Some patients might have their test result almost one day earlier than previously. The staff was accustomed to clinical microsystems. The implementation process proceeded well. Difficulties sometimes arose as a result of unexpected events after the improvement. This was for instance observed after introduction of RAST as more work had to be done in the afternoon and the personal resources had to be rescheduled. The MALDI ToF typing system is now in use also for bacterial samples from other parts of the body, and thereby typing results may be even more reliable as only one method is used for a given bacteria.

A preliminary report with bacterial type and the result of RAST is now sent the same day as a blood culture bottle has indicated growth. Before the intervention this was not done until the next day. The patients with inadequate treatment might therefore more rapidly get appropriate treatment. This may result in less suffering and a higher degree of patient survival (Hanlon et al., 2002). Furthermore, the treatment with broad spectrum antibiotics can be shortened (Kerremans et al. 2008), which hopefully leads to reduced development of antibiotic resistant bacteria.
We found that the staff very well could handle the changes brought by the improvement. The change from traditional biochemical typing used for over 50 years in the clinical Microbiological in Jönköping, to MALDI ToF was a paradigm shift. Nobody of the interviewees was disappointed that some of the most fundamental microbiological routines were laid to rest.

**Relation to other evidence**

**The improved blood culture process**

Customer satisfaction is important and one important indicator of the quality of care is TAT for a clinical sample referred to a laboratory (Howanitz 2005). Reducing the TAT for patients with resistant bacteria is important. After adjusting for risk factors, patients receiving a treatment that covered the microorganism(s) had an increased survival (Hanon et al., 2002). In another study adequate antibiotic treatment had an impact on survival only if it was started within the first 24 hours after the blood culture sample was drawn (Mathevon et al. 2002). For patients in Jönköping County with CTX: R enterobacteriaceae 2011 more than 50% had received inadequate antibiotic treatment, thus the reduction of the time from a positive blood culture to the response of susceptibility testing from 25 hours to six hours by implementing the RAST method is highly relevant. Our figures also confirm the results by Trenholme et al. 1989 who documented that their AST results were available within an average of nine hours by the direct method versus 48 hours by the routine method. Pedersen et al. 1997 showed that in 16% of patients with bacteraemia, antibiotic treatment was not instituted before notification of a positive blood culture and in 9% empirical antibiotic treatment was inappropriate.

Rapid bacterial identification and susceptibility testing in blood cultures has been shown to lead to a more rapid switch to proper antibiotic treatment and to a significant reduction in antibiotic use (Kerremans et al. 2008). Also a change to more effective therapy or to less expensive antibiotics was observed (Trenholme et al. 1989). The key factor for patients with CTX: R enterobacteriaceae to get adequate antibiotic treatment is the direct contact from the laboratory. Each time the laboratory physician called and reported the results the patient received adequate treatment the same day. In weekends when no physician is in service at the laboratory a new improvement would be that biomedical technologists perform the phone reporting, when a patient with CTX: R enterobacteriaceae without adequate antibiotic treatment is observed.

Faster reporting of identification and AST results was found to be associated with a significant reduction in hospital stay and in overall cost for patients where wound, abscess, and urine specimens were analyzed (Galar et al. 2012). The introduction of MALDI ToF in Jönköping reduced the TAT for the identification of bacteria of many species with at least one day which hopefully reduce hospital stay and the cost for some of these patients.

The TAT has also an impact on length of hospital stay. Barenfanger et al. showed that the average length of stay was 11 days per patient when rapid bacterial identification and AST was used versus 13 days for the others (Barenfanger et al. 1999). In another study patient costs for hospitalization were significantly lower in the rapid test group (Doern et al. 1994). However, in a recent study the rapid antimicrobial results of blood cultures did not lead to significant clinical or financial benefits (Galar et al. 2012). In one study rapid bacterial identification and susceptibility testing, in blood culture, did not reduce mortality (Kerremans et al. 2008), but in another mortality rates were lower in the rapid test group (9% versus 15%) (Doern et al. 1994). After implementation of RAST in our study the average time from sampling to susceptibility testing was 43 hours for patients with CTX: R enterobacteriaceae and the minimal time observed was 24 hours and 18
minutes. If the process is changed and the TAT from sampling to susceptibility testing reduces to 24 hours or less, the clinical microbiology laboratory could play a key role for the patient survival (Mathevon et al. 2002). This however, requires nightshift which will be very expensive. A more reasonable act might be to start laboratory work earlier in the morning to make possible that the results will be given before the patient responsible clinician leave for the day. Another improvement might be to let the two biomedical technologists culturing new samples between 4 PM and 6 PM to also process blood cultures.

**Staff experience of change**

The staffs at clinical microbiology and clinical chemistry in Jönköping were satisfied with their work. Varkey et al found that in an institution that had implemented clinical microsystems, employees felt more satisfied than in the institutions where the concept and understanding of clinical microsystems were not implemented (2008). Individuals at each organizational level have unique and critical roles to play in implementing and sustaining quality improvements efforts (Kichner et al. 2012). The codes in the category “driving forces” were “to develop”, “to learn more” and “to obtain better outcomes”. The leadership in the two clinics seems, however, to be different as the staff at the clinical microbiology laboratory indicates that they can make their own decision to change. Some of the interviewed staff at clinical microbiology laboratory said “we have the opportunity to do changes without asking the leadership” while some of the interviewed staff at clinical chemistry said “you always have to ask the leadership”.

The codes in the category cooperation were “cooperation in the blood culture process” and “barriers for cooperation”. In 2005, clinical chemistry laboratory and clinical microbiology laboratory were located together. The management made it clear that cooperation between the departments should increase. Numerous attempts to increase integration between departments have been made. Some of the staff at the clinic chemistry laboratory have learned to cultivate the bacterial samples and perform serological analyzes. Today, the same instruments are used by both departments, but chemical analyzes are done by clinical chemistry staff and microbiological analysis are done by the clinical microbiology staff. In the interviews of the staff several said that the integration problem was due to different laboratory information systems (LISs). In 2012, the LIS for the two departments will be the same and no longer a barrier for cooperation.

The codes in the category “patient foci” were: “faster response” and “more correct response”. Some of the staff felt a bit strained when RAST was introduced. Working with RAST meant another operation to be carried out during the first hours of the working day when they already had plenty of work to do. During the first two months data were collected for validation of the method. In this period the staff also learnt how to execute the RAST. After discussion with the clinical physicians it was decided that the RAST should be ready until 4 pm and the change in antibiotic therapy can then be done by the physician at the day shift.

The codes in the category “changed knowledge” were: “tacit knowledge will be forgotten” and “less opportunities for verifying”. The MALDI ToF is rapid and uncomplicated to use. After MALDI ToF was introduced there is less opportunities to verify the bacterial species than with the previous typing methods. In the conventional typing methods often one test was for the genus level and another biochemical test was used for the species level. One problem may be when the machine breaks down and biochemical tests are no longer in stock. It will take many days until all the biochemical tests are in production. Some of the test batteries can be stored in the freezer but others containing agar are not possible to store. Collaboration with other clinical microbiology laboratories in the region could solve this problem.
In the interviews of the staff at the clinical microbiology laboratory the experience was that patient safety should increase when typing using MALDI ToF was introduced. Earlier there was one battery of biochemical test for isolates obtained from wounds and another for isolates from urine which might result in discrepant results. With MALDI ToF bacteria found in different sites of the body will be typed with the same method. One concern is that new employees will lack basic knowledge in bacteriology. You learn it when you are student but working is a continuously learning and hopefully the old knowledge will not be forgotten.

**Limitations**

There is no nationwide definition of sampling time. This might result in misleading results from inter-laboratory comparison of MQI data. Another limitation in the MQI-comparisons was that data collection only was performed during two weeks in September and October. To notice changes in process observations will be done monthly. To analyze the clinical perspective the time from sampling to adequate treatment for patient with CTX: R enterobacteriaceae in blood culture who lack adequate treatment was measured. The time after implementation was however too short and only one patient with lack of adequate treatment was found and therefore the result is unreliable. In the pre-analytic phase only the clinic with the most samples was included, hopefully more clinics will be included in the future.

**Interpretation**

During the last few decades we have seen a significant decrease in the rates of analytical errors in clinical laboratories, and currently available evidence demonstrates that the pre- and post-analytical steps of the total testing process are more error-prone than the analytical phase (Plebani 2009). The pre- and post-analytical phases were found to constitute 75 % to the total TAT. The TAT demonstrates the need for improvement in the pre- and post-analytical periods (Goswami et al. 2010). Transportation times from the two remote hospitals: Highland Hospital in Eksjö and Värnamo Hospital are long. In the future more improvements have to be done to reduce this part of the TAT. The idea to place incubators at the clinical chemistry laboratories in Eksjö and Värnamo is under discussion. The positive blood cultures bottles will then be sent to Jönköping for final analyses. Risk assessments must, however, be done before such a change. The time from sampling to incubation will hopefully be reduced but the TAT for positive bottles has to be measured.

“Archaeological laboratory results or microbiology in time?” was the question. To be “microbiology in time” the focus on continuous improvements plays a crucial part. Collaboration with clinical departments to improve the pre- and post-analytic phase has to be intensified. Rescheduling the staff working time to start with the blood cultures earlier in the morning and also to work with the blood cultures later in the evenings may further reduce TAT. More efficient transport within and between hospital is one of the most important factors today.

**Conclusions**

The two study questions of this thesis were:

- How can the blood culture process be improved, with decreased TAT, to make faster adequate treatment of the patient possible?, and
- What are the perceived staff experiences of the changes performed in order to improve the blood culture process?
The blood culture process was improved by re-design during evenings and nights and typing with MALDI ToF and RAST with the disc diffusion method were introduced to improve the TAT. The TAT from sampling to incubation at the County Hospital Ryhov has decreased from six hours to two hours and 21 minutes. The TAT at the two remote hospitals from which blood cultures are transported has decreased from 16 to 11.5 hours in Highland Hospital in Eksjö and 20 to 13 hours in Värnamo Hospital, respectively. The time from sampling to RAST and typing with MALDI ToF for patients with CTX: R enterobacteriaceae was reduces from 55 to 43 hours and the minimum time registered was 24.3 hours. This means that patients with inadequate treatment can be treated earlier and the treatment with broad spectrum antibiotics can be minimized, which hopefully will lead less development of resistant bacteria, less suffering and a better patient survival.

Staff experiences of the improvement project were mostly positive. The study of the implementation of the improvements showed that the staff of the clinical microbiology and clinical chemistry laboratory could handle the change brought by the improvement project very well. The change from traditional biochemical typing that has been used for over 50 years, to MALDI ToF was indeed perceived as a paradigm shift. The staff deemed themselves lucky to be able to experience such a revolution. Nobody was disappointed that some of the fundamental microbiological laboratory working routines was laid to rest. The driving forces of the quality improvement where to develop, learn, and obtain better outcomes, such as safer and faster results. Barriers for the quality improvement project were the working times and the transportation time of blood culture samples. Important categories found in the interviews were patient foci, changed knowledge, cooperation and driving forces. Implications for practice were that this study could help other laboratories to improve the process by implement new methods and cooperation between departments to reduce TAT from sampling until the patient received adequate treatment. The staff interviewees increase the understanding of experiences to changes which could enable continuous learning and other quality improvement in health care. In doing this, it is important to consider a patient focus, and to enhance learning and cooperation.

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References


Appendices

Appendix 1. Interview guide

Interview of staff in clinical microbiology laboratory

Purpose:
For what purpose did you think that MALDI ToF was bought?
What was the purpose when "rapid susceptibility testing" was introduced?

Patients/Clients:
How will the customer notice the change?
Does it affect patient safety by MALDI’s introduction?
Does it affect patient safety by the introduction of "rapid susceptibility testing"?

People/Employees:
How do you feel about the clinic is going to abandon many of the biochemical tests?
How have you been involved in MALDI ToF’s introduction?
Do you feel stressed to make rapid susceptibility testing before 10 AM?

Processes:
How is the procedures changed when MALDI ToF and rapid susceptibility testing are introduced?
How is the response time changed?
How will your knowledge of typing bacterium change?

Pattern:
How will the variation be influenced by MALDI ToF?
What will the workflow be like with untyped bacterial strains by MALDI ToF?
Rapid and conventional susceptibility testing has different zones. How can it be affected?

Driving forces:
How do you like your job?
What is it that motivates you? What is less motivating?
What are the incentives to develop your work?
Interview of staff in clinical chemistry laboratory:

Purpose:
What was the purpose you perceived when you were asked to place blood culture bottles in the incubator?

Patients/Clients:
How will the customer notice the change?

People/Employees:
How are you affected by this new operation?

Processes:
How has this operation changed the routines of the evening and weekend work?

Pattern:
Are there any times of day when it’s harder to keep up to care for blood cultures?

Driving forces:
What are the driving forces to develop cooperation between the clinical microbiology laboratory and clinical chemistry laboratory?
### Appendix 2. The qualitative analysis

<table>
<thead>
<tr>
<th>Quotation</th>
<th>Condensing</th>
<th>Codes</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>The purpose was faster response to the patients</td>
<td>The purpose was faster response</td>
<td>Faster response</td>
<td>Patient focus</td>
</tr>
<tr>
<td>The patient safety would be better with one instrument.</td>
<td>The safety would be better</td>
<td>More correct response</td>
<td>Patient focus</td>
</tr>
<tr>
<td>New employees would lack basic way of thinking in bacteriology</td>
<td>New employees will lack knowledge</td>
<td>Tacit knowledge will be forgotten</td>
<td>Changed knowledge</td>
</tr>
<tr>
<td>There is less opportunities to verify the bacterial species compared with the previous typing methods</td>
<td>There is less opportunities to verify the bacterial species</td>
<td>Less opportunities for verifying</td>
<td>Changed knowledge</td>
</tr>
<tr>
<td>The incubating of the blood cultures doesn’t take long time to perform</td>
<td>The incubation is easy to perform</td>
<td>Cooperation in the blood culture process</td>
<td>Cooperation</td>
</tr>
<tr>
<td>Today, it is watertight bulkheads between the departments and also in the leadership”</td>
<td>We didn’t work together</td>
<td>Barriers for cooperation</td>
<td>Cooperation</td>
</tr>
<tr>
<td>It is evolving to test new things on my own workplace.</td>
<td>The changing is evolving</td>
<td>To develop</td>
<td>Driving forces</td>
</tr>
<tr>
<td>One motivator is to learn new things</td>
<td>It is motivating to learn new</td>
<td>To learn</td>
<td>Driving forces</td>
</tr>
<tr>
<td>One driving forces is to obtain better, more reliable and faster results.</td>
<td>One driving forces is to obtain better outcomes</td>
<td>To obtain better outcomes</td>
<td>Driving forces</td>
</tr>
</tbody>
</table>