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Case report

Enhanced diagnostics of pyelonephritis - A case report

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A case of 49-year-old man with a pyelonephritis occurring for the second time within a year is described with special emphasis to the urgent verification detection of the urinary pathogen. The patient was treated in Kuopio University Hospital (KUH), Finland. An Uricult dipslide method (Orion Diagnostica Oy, Espoo, Finland; standard method) was compared with a PMEU Scentrion® enrichment culture method (PMEU method), where the growth of the bacteria was detected by the PMEU Scentrion® analysis of volatiles emitted from the syringes. By the PMEU method the bacterial growth was detected after 3 h with equal speed from both aerobic and anaerobic enrichment cultures. By the standard method one day after the sampling, when the plates were read for the first time, the pathogen concentration was >10E5/ ml. The enhancement of microbiological analysis of urine samples is warranted for decreasing the numbers of complications. This is especially important for patients prone to urinary tract infections or at risk of disseminating antibiotic resistant strains. According to this study the PMEU method proved out to be a useful means for shortening the delays and in guiding the selection of suitable treatments for urinary tract infections repeatedly threatening a risk patient.

Key words: Pyelonephritis, *Escherichia coli*, enrichment culture, rapid microbial detection, portable microbe enrichment unit (PMEU), urinary tract infections.

INTRODUCTION

Urinary tract infections (UTI's) are the most common infectious diseases causing substantial amount of morbidity among all age groups (Bhat et al., 2011; Foxman, 2010; Matthews and Lancaster, 2011). The symptoms of the UTI depend on the level of the infection. The classical symptoms of cystitis are dysuria, pollakisuria and lower abdominal pain, but more severe form of UTI, pyelonephritis, is characterized by acute onset of infectious symptoms like fever, fatigue, deterioration of general condition and pain in the back and/or side of the body close to the location of kidneys. If not treated properly the pyelonephritis may also develop to urosepsis that is a septichaemic condition originating from the urinary tract.

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Early diagnosis of the causative agent of UTI is important. For practical reasons an empiric antibiotic treatment is often introduced because it normally takes 1 to 2 days until the results of the bacterial cultures of the urinary samples are available and further 24 h before the antibiotic resistance data is completed. Identification of the pathogens and the analysis of their antibiotic resistance patterns guide the physicians in the clinical evaluation of the UTI and in the selection of the proper antibiotic treatments for the patients. It would be of great importance to effectively shorten the duration of microbial diagnostics in order to reduce the human suffering and cut the costs for the health care system. Economical savings could also be achieved as a result of shortened sick-leaves, and by the decrease in severe, hard to treat complications of the UTI.

The portable microbe enrichment unit (PMEU) technology has been developed for enhanced recovery

and growth of various microbes (Hakalehto, 2010). It has been used for the detection of septic bacterial strains (Hakalehto et al., 2009), infantile fecal enterobacteria (Pesola et al., 2009) and *Campylobacter* sp. strains (Pitkänen et al., 2009). PMEU method is also suitable for monitoring the antibiotic susceptibilities of different hospital strains (Hakalehto, 2011a, b). This enhanced enrichment procedure has been applied for the follow up of a maturing microbiota of an infant during - and in spite of - numerous antibiotic treatments (Pesola and Hakalehto, 2011).

The PMEU cultivation of for example, salmonellas was shown to take place with an identical speed both in aerobic and in anaerobic culture mode (Hakalehto et al., 2007). PMEU Scentrion® has been developed in order to further enhance the detection of microbes in different samples on the basis of their volatile emissions (Hakalehto et al., 2009). Samples are incubated in syringes inside the PMEU where the growth conditions are optimized (temperature, gas atmosphere, availability of nutrients). The samples are mixed by funneling sterile filtered gas inside the samples. The microbial growth is monitored by detection of volatiles emitted from the samples in the outlet gas flow. The validation studies of this PMEU method are going on in the Kuopio University Hospital (Pesola et al., 2011).

Hereby we describe a case with pyelonephritis. In the microbial diagnostics the PMEU method was used in addition to the routine microbiological tests.

CASE PRESENTATION

49-year-old man was admitted to Kuopio University Hospital (KUH), Finland, in January 2011. He had earlier in 2008 been treated in the KUH because of severe acute pyelonephritis caused by a *Citrobacter* sp. strain containing some antibiotic resistant markers.

About 12 h before the admission the patient had got fever and back pain. Then urine was turned non-transparent. In the clinical examination the percussion of the back provoked pain bilaterally and diffuse abdominal pain was detected by the palpation.

During admission the leukocytes of the peripheral blood were 12.2 × 10E9/l, neutrophilic granulocytes 10.6 × 10E9/l, hemoglobin 141 g/l, thrombocytes 208 × 10E9/l, C-reactive protein (CRP) 33 mg/l and creatinine 78 µmol/l. 24 h later the C-reactive protein (CRP) had increased to 197 mg/l, leukocytes to 16.7 × 10E9/l and creatinine was 104 µmol/l.

The results of urinalysis: the number of leukocytes >30, erythrocytes 1 and epithelial squamous cells 1 / microscopy field, nitrite negative, albumin negative, glucose negative, pH 8.0.

Because of clinical signs of acute pyelonephritis, cefuroxime was introduced after the collection of urinary and blood culture samples.

Both two blood cultures taken during admission before the introduction of the antibiotic treatment were answered negative.

Two days after the onset of antibiotics the leukocytes were 7.2 × 10E9/l, CRP 126 mg/l and creatinine 89 µmol/l. Then the CRP declined rapidly being 10 mg/l after five days of antibiotic treatment, when the patient was discharged.

The bacterial culture of the urinary sample was performed by two different methods with and without the PMEU enrichment as described as follows:

1. The bacterial culture of the first subsample was examined by the standard method of the Eastern Finland Laboratory Centre Joint Authority Enterprise (ISLAB, Kuopio, Finland), that is based on the use of Uricult dipslide method (Orion Diagnostica Oy, Espoo, Finland; standard method). One side of the Uricult slide is covered by cystine-lactose-electrolyte-deficient (CLED) medium, while the other side is covered by MacConkey medium.

The Uricult slide was dipped in the urine sample and then incubated in upright position for 24 h in +36 +/- 2°C. Then after the bacterial counts were estimated. Further cultures were performed for the antibiotic resistance monitoring on Müller-Hinton agar plates. After incubation of 24 h in +37°C the antibiotic resistance pattern was interpreted.

2. The other subsample was cultivated in the PMEU Scentrion® (Figure 1). Firstly, 7 ml of BacT/ALERT® FA culture medium (bioMérieux, France) was aspirated to one 20 ml syringe (aerobic sample syringe) and 7 ml of BacT/ALERT® SN to another 20 ml syringe (anaerobic sample syringe). Secondly, 5 ml of the subsample was taken to both syringes, and the syringes were connected to the PMEU. There the enrichment culture took place in specific syringes containing broth medium. Gas flow of sterile filtered ambient air was directed into aerobic syringes and anaerobic gas (N_2 90%, CO_2 10%) into anaerobic syringes through sterile filters (0.2 µm, SY13TF-S, Advanced Microdevices Pvt. Limited, Ambala Cantt, India) and needles (0.80 × 120 mm, Sterican, B. Braun Melsungen AG, Melsungen, Germany) in order to agitate the broth and the bacterial cells. All samples were incubated in +35°C.

When an alert of microbial growth was detected by either method, Gram-staining, plate culture, identification and antibiotic susceptibility testing of the strains were performed by standard methods in Eastern Finland Laboratory Centre Joint Authority Enterprise (ISLAB, Kuopio, Finland).

The *E. coli* growth was detected after 3 h in both aerobic (Figure 2) and anaerobic (Figure 3) enrichment cultures using the PMEU method. The growth was observed by the PMEU Scentrion® analysis of volatiles emitted from the syringes (Figure 4). The bacterial production of volatiles was much stronger and long lasting in the case of anaerobiosis.

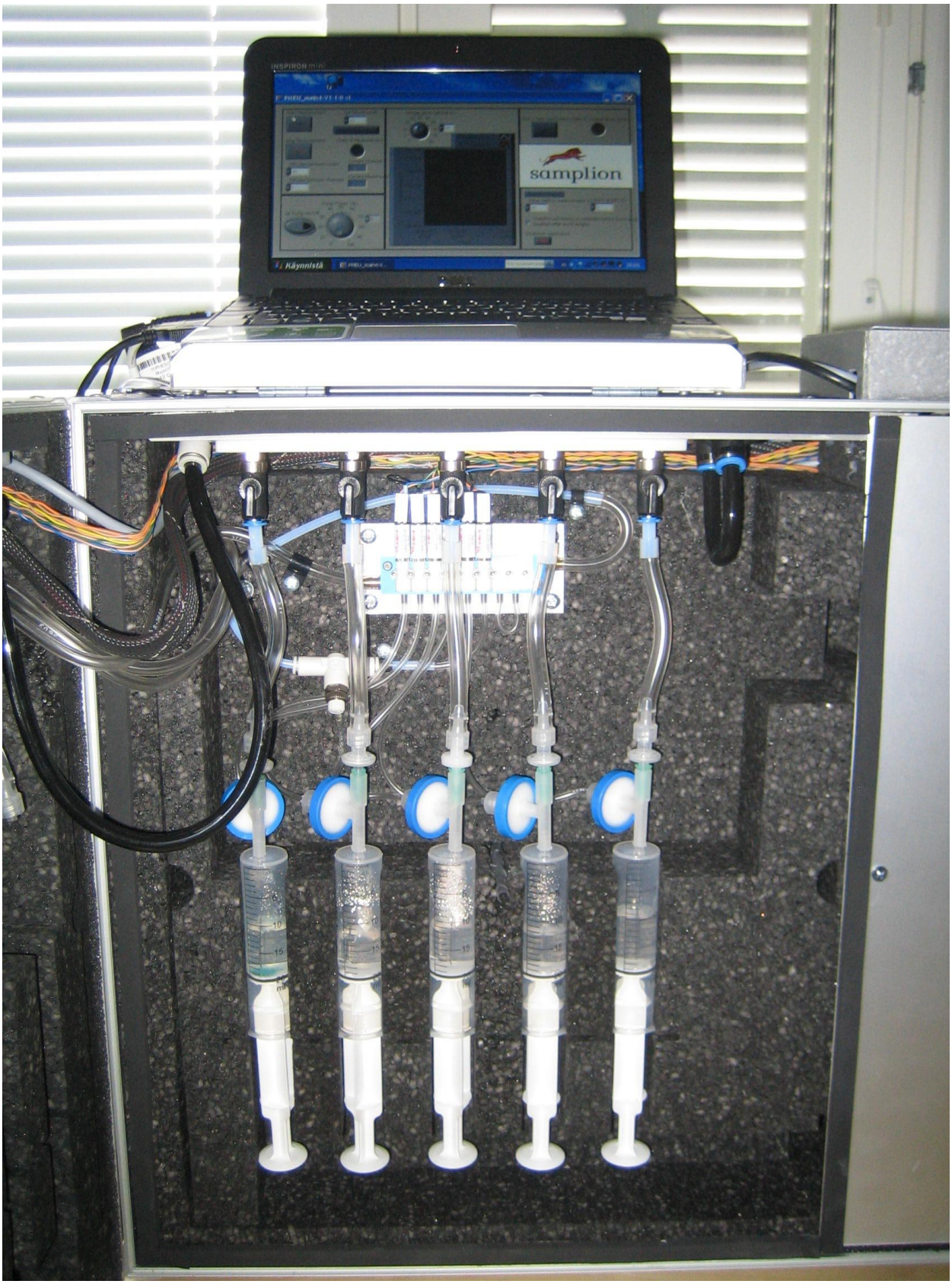

Figure 1. PMEU Scentrion® (portable microbe enrichment unit; Finnoflag Oy, Kuopio and Siilinjärvi, Finland; Samplion Oy, Siilinjärvi, Finland).

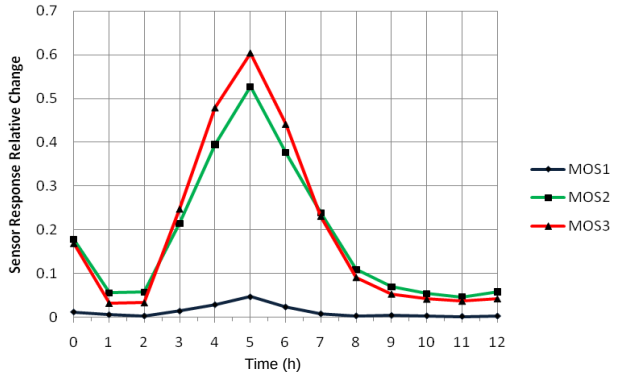

Figure 2. Aerobic cultivation in the PMEU Scentrion®. The bacterial emissions detected by metal oxide sensors MOS1-3 (Hakalehto et al., 2009; Hakalehto, 2010).

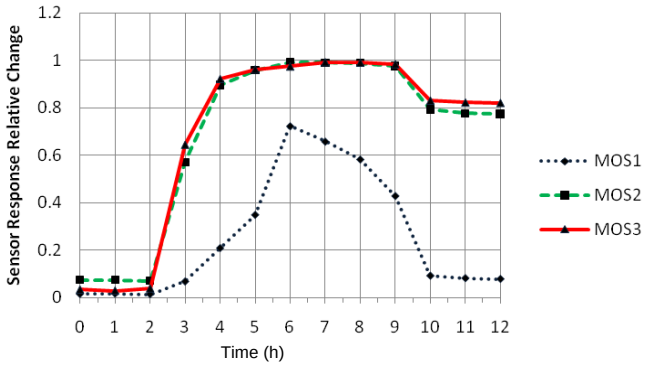

Figure 3. Anaerobic cultivation in the PMEU Scentrion®. The bacterial emissions detected by sensors MOS1-3.

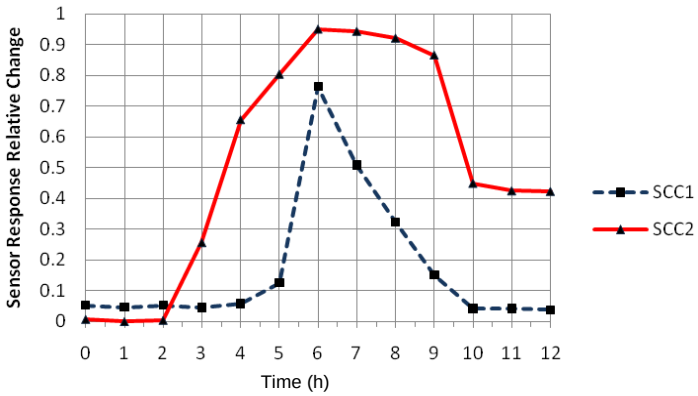

Figure 4. Anaerobic cultivation in the PMEU Scentrion®. The bacterial emissions detected by semiconductive sensors SCC1-2.

On the day 1 after the sampling, the number of the pathogen was >10E5/ ml, according to the standard method.

By both culture methods the same bacterium causing UTI's, *E. coli*, was detected. The species of the bacterium and results of the antibiotic resistance tests were

answered two days after the sampling.

The bacterial strain was shown to be sensitive to all tested antibiotics: ampicillin, cefalexin, cefuroxime, mesillinam, nitrofurantoin, norfloxacin and trimetoprim. The patient had got a year earlier urinary infection caused by *Citrobacter* sp. which carried some resistance markers. Now sign of transformation of these markers was observed.

DISCUSSION

In this study the PMEU Scentrion® increased remarkably the speed of achieving the information on the bacterial growth from the urinary samples. The growth was detected as early as after three hours of the PMEU cultivation. By standard method this result is normally got only after 24 h of cultivation on the Uricult slide.

PMEU Scentrion® device and the corresponding enrichment method were used parallel to the standard method in culturing of the bacterial strains in urinary sample. According to the results from both methods the same pathogenic *E. coli* strain was detected.

Growth of the facultatively anaerobic member of the family *Enterobacteriaceae* was detected equally fast by both aerobic and anaerobic procedures when the PMEU technology was used for the verification. This observation is in line with the earlier studies regarding the speeding up of growth in anaerobiosis (Hakalehto et al., 2007; Hakalehto, 2011a). In this study the peak gas formation occurred after 5 h of cultivation aerobically, and in 5 to 6 h anaerobically.

In the former the measurable effect lasted up to 8 h from the onset of the culture, whereas in anaerobiosis it lasted up to 10 h time point, at least.

In an earlier episode of the pyelonephritis a year earlier the same patient was having a level of CRP of about 90 mg/l by admission, and the antibiotic treatment was started about ten hours later (results not shown here). As a result of this delay, the CRP reached 290 mg/l the next morning. In this latter outbreak of infection the antibiotic medication was started earlier which resulted in lower CRP values, and more importantly, in shortened duration of illness. This difference between the UTI episodes indicates also the importance of earlier detection and identification of the infective agent, which was in this test case produced by the implementation of the PMEU Scentrion® system into the emergency department. This kind of approach could not only improve the health prognosis of a particular patient, but is also economically beneficial for the entire hospital organization, as the costly period required for diagnostics is being shortened (Hakalehto, 2011b).

The identification of the bacterial species and antibiotic resistance tests were answered two days after the sampling. These analysis procedures were carried out by the conventional methods in this experimentation. However, the PMEU approach has also turned out to be effective in the monitoring of antibiotic resistant bacterial strains. In a recent study, the antibiotic resistances of an *Enterobacter cloacae* strain were detected using an infrared sensing (IR) sensing PMEU version, PMEU Spectrion® (Hakalehto, 2011b).

Means for enhanced detection of urinary pathogens are needed for every patient with UTI's, but they are especially important for urosepsis patients (Wagenlehner et al., 2011) and groups of people prone to severe UTI's, that is, children with congenital malformations of urinary tracts (Routh et al., 2010; Winyard and Chitty, 2008), catheterized patients (Wagenlehner et al., 2012), people with neurogenic bladder causing retention of urine in the bladder and prolonged need of repeated bladder catheterizations (Gormley, 2010), and immunocompromised patients (Neal, 2008). The patient in this case study had a chronic back problem, which quite often led to catheterization. Also pregnancy, diabetes and renal calculi increase the risk of complicated acute pyelonephritis (Shields and Maxwell, 2010).

This case report gives interesting insight into the potential that the PMEU Scentrion® has in the microbial analysis of urinary samples. Swift monitoring of samples is important in order to prevent urosepsis and other complications (Wagenlehner et al., 2011). A pyelonephritis should always be suspected and excluded when febrile infants are seen, because the symptoms of the infantile UTI are very unspecific and their immature immunity increase the risk of UTI's (Feld, 1991). This emphasizes the need for novel fast methods for their verification. The PMEU technologies can be linked with a real-time follow up by the internet or wireless connections. This procedure is giving the physicians direct information on the growth of the microbial isolates, when the PMEU is situated either in the laboratory or in the hospital ward (Hakalehto, 2010).

Conclusions

Rapid pathological development of the pyelonephritis requires alerted preparedness in case of all patients, and especially with respect to the neonates and the elderly, as well as many types of chronically ill patients. The PMEU method proved out to be a useful means for shortening the delays in starting the correct treatments for preventing the infections. It makes the verification of the pathogen in a few hours only. This is also lowering the expenses in the hospital wards, as the patients are recovered more rapidly. The PMEU versions can also be used for the monitoring of the antibiotic resistant traits of the pathogens. This eventually assisted in selecting correct antibiotic medication for various patient cases. Also the follow up of the effects of the antibiotic treatment and other cure could be screened quickly with the PMEU

enhanced enrichment.

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