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Fast Indication of Bacterial Growth in Clinical Specimens by the PMEU Approach

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Fast spreading microbial diseases warrant rapid diagnostics. PMEU (Portable Microbe Enrichment Unit, developed by Finnoflag Oy, Finland; Fig. 1) has been used for rapid microbial diagnostics. The unit is suitable for fast-spreading infections (Hakalehto 2012, 2015; Pesola et al. 2012) and for detection of latent or slow-growing bacteria, *e.g. Mycobacterium* spp. (Hakalehto 2013, 2014; Hakalehto et al. 2015), as well as for characterization of intestinal microbiota (Pesola et al. 2009). Antibiotic resistance can been screened successfully within a few hours using the PMEU (Hakalehto 2014). This could facilitate fast decisions during treatment of critical infections.

Neonatal and neutropenic septicaemias are important causes of treatment related morbidity and mortality in paediatric patients. However, blood cultures are positive in only 10-20% of the cases. Also in many other critical infections real pathogens often remain undetected. Small sample size, low microbial concentrations, demand of anaerobiosis and poor cultivability of some pathogens cause problems in rapid verification of microbes. Therefore, developing new methods providing early warning of the infective agents are valuable, because accurate and timely diagnosis is essential for survival (Laitiomäki 2014).

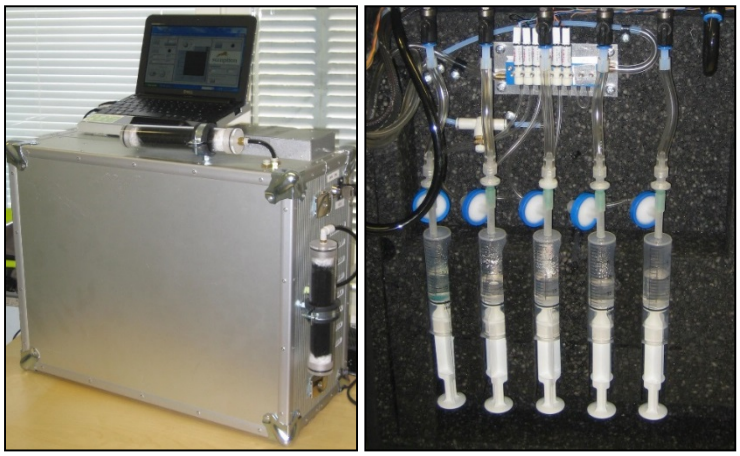

Figure 1. PMEU Scentrion® is a hybrid analyzer designed by Adj. Prof. Elias Hakalehto (Finnoflag Oy) and Dr. Heikki Paakkanen (Environics Oy).

In the PMEU samples are incubated in syringes inside the device where the growth conditions, *i.e.* temperature, gas atmosphere and availability of nutrients, are optimized. The samples are mixed by

funneling sterile filtered gas inside the syringes. In the PMEU Scentrion® microbial growth is monitored by detection of vapors emitted from the samples (Pesola *et al.* 2012).

In an on-going study the PMEU Scentrion® is compared with a standard BacT/ALERT® blood culture device (bioMérieux, France) in the enrichment of paediatric blood cultures (Laitiomäki 2014). Patients are recruited at the Neonatal Intensive Care Unit and Pediatric Haematology and Oncology Ward of Kuopio University Hospital in Kuopio, Finland. When any microbial growth is detected after aerobic or anaerobic incubation by either method, Gram-staining, plate culture, identification and antibiotic susceptibility testing of the strains are performed by standard methods in Eastern Finland Laboratory Centre Joint Authority Enterprise (ISLAB, Kuopio, Finland). So far, 61 neonatal and 43 hematological cases have been studied. The numbers of isolated microbial strains and detection time appear to be fairly similar by both methods complementing each other.

In case of urinary tract infection samples were enriched in PMEU Scentrion®. By this approach *E. coli* was detected as a cause of pyelonephritis within 3 hours cultivation (Pesola et al. 2012). Mycobacterial strains were enriched using Middlebrook 7H9 (Difco) broth. Fast-growing species, such as *M. fortuitum,* were detected in less than 12 hours. Slow-growing strains like *M. marinum* were detected in 2 days instead of several weeks usually needed for the verification (Hakalehto 2013, 2014; Hakalehto et al. 2015). Regardless of the sample type the PMEU Scentrion® has shortened the detection time and enhanced the accuracy of the analyses. The method has promising potential in analyzing blood culture and other clinical samples in a comparable fashion with the standard methods. It could also reveal hiding contaminants, especially the anaerobes. The method is feasible both for laboratories and even bed-side at the ward, giving real-time alarms of bacterial growth, also in latent infections. It is also possible to rapidly screen the antibiotic resistance patterns on the cultures in order to guide the selection of appropriate antibiotic therapies.

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