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Severe *plasmodium falciparum* malaria in an asplenic traveler

D.T. Nguyen, L.S. Slobbe, P.J.J. van Genderen, J.J. van Hellemond
Department of Medical microbiology and Infectious Diseases, Erasmus MC, Rotterdam, the Netherlands

Malaria caused by *Plasmodium spp.* still has a huge global burden with estimated 438,000 deaths. *Plasmodium falciparum (Pf)* causes the largest burden, ranging from uncomplicated to severe malaria and death. *Pf* infected-erythrocytes have the ability to adhere to endothelial cells of blood vessels by expressing surface receptors, thereby escaping removal by the spleen. In this presentation we present an asplenic traveler returning from a malaria endemic country. During his stay he did not use any malaria prophylaxis. Back home he developed fever and headache. Thin smear showed *Pf* trophozoites and one schizont. The diagnosis was severe malaria tropica with a parasitaemia of 10.2%, which requires intensive care according to WHO criteria. In contrast to this parasitaemia he did not demonstrate any clinical symptoms of severe malaria. We showed that the time to clear parasites after initiation of therapy was extended. Moreover, his parasitaemia was prolonged up to almost one month as visualized by thin smears and confirmed by nucleic acid amplification tests. Interestingly, after four days of therapy thin smear analysis still showed an intact trophozoite. Other studies of malaria infected asplenic patients showed that *ex vivo* cultures of such trophozoites were not infectious. In addition, studies illustrated that *Pf* infected-erythrocytes in an asplenic patient do not express surface antigens, thereby strongly reducing sequestration and organ damage. We conclude that in asplenic patients a parasitaemia > 5% does not always indicate severe malaria and asplenic patients need a longer follow-up since parasitaemia is prolonged.

Data have been presented during WAMM/NVP meeting on September 18th 2018

Post-operative yeast infections after esophagectomy: a retrospective study at the University Medical Center Groningen

M. Heuker[1*], U. Koser[2*], A. Ott[3], A. Karrenbeld[4], J.M. van Dijl[1], G.M. van Dam[2,5], A.M.G.A. de Smet[2], M. van Oosten[1].*Both authors contributed equally to this work.
[1]Department of Medical Microbiology, University of Groningen, University Medical CenterGroningen, the Netherlands; [2]Intensive Care Unit, University of Groningen, University Medical Center Groningen, the Netherlands; [3]Department of Medical Microbiology, Certe, Groningen, the Netherlands;[4]Department of Pathology, University of Groningen, University Medical Center Groningen, the Netherlands;[5]Department of Surgery, Division of Surgical Oncology, University of Groningen, University Medical Center Groningen, the Netherlands

Esophagectomy is an operative intervention with high morbidity and mortality. Pulmonary infection is one of the largest determinants of postoperative morbidity after esophagectomy and often originates from microorganisms of the oropharyngeal flora, as this phenomenon is caused by leakage of the cervical anastomosis. It has been shown that selective decontamination of the digestive tract (SDD) and selective oropharyngeal decontamination (SOD) are able to reduce the incidence of (pulmonary) infection and anastomotic leakage, and improve survival in surgical critical care patients. However, currently it is unknown to

what extent yeast play a role in post-operative infections in esophagectomy patients and if antifungal therapy should be added to the SDD regimen in this patient group. In this study, we analysed the prevalence of yeast infections in patients following esophageal resection at the University Medical Center Groningen.
A retrospective analysis of all esophagectomy patients between January 1991 and July 2017 was performed, with a total of 566 patients analysed. Institutional review board permission for this study was obtained and all collected data was treated pseudo-anonymously and in adherence to the Declaration of Helsinki. A division was made between patients who developed a yeast infection after surgery and those who did not. Several patient characteristics and microbiological cultures were identified.
Based on the present findings, we conclude that 7% of patients developed a yeast infection after esophageal resection. Moreover, patients with diabetes mellitus developed significantly more yeast infections and therefore, may be at higher risk. This study supports the consideration of investigating the inclusion of antifungal treatment in the SDD regimen for patients undergoing esophagectomy.

Ex vivo imaging of osteomyelitis and implant infections using fluorescently labelled vancomycin

M . López-Álvarez[1*], M. Heuker[1*], G.M. van Dam[2,3], J.M. van Dijl[1], F.F.A. IJpma[2#], M. van Oosten[1]
*,# These authors contributed equally to this work.
[1]Department of Medical Microbiology, University of Groningen, University Medical Center Groningen, the Netherlands; [2]Department of Surgery, University of Groningen, University Medical Center Groningen, the Netherlands; [3]Intensive Care Unit, University of Groningen, University Medical Center Groningen, the Netherlands

Osteomyelitis and implant infections are severe complications after bone fracture treatment. Clinical suspicion usually results in surgery. However, there is no adequate tool during surgery to directly distinguish osteomyelitis or implant infections from sterile inflammation. Moreover, a definitive preoperative diagnosis is often not possible. This can lead to treatment delays or overtreatment, which culminate in poorer outcomes and multi-resistant bacteria.
Early and accurate visualization to discriminate between infection and sterile inflammation and to identify the causative pathogen will substantially improve clinical decision-making. Therefore, we aim to establish a bacteria-targeted imaging approach to discriminate between infected materials (such as tissue, bone marrow and biomaterials) and non-infected materials during surgery. This will provide real-time fast and accurate information, leading to a better diagnosis and treatment.
A promising molecular imaging approach for the specific detection of Gram-positive bacteria is based on a near-infrared fluorescently labelled vancomycin, vancomycin-IDRye800CW. Vancomycin is a glycopeptide antibiotic drug that selectively binds to the D-Ala-D-Ala moiety in the Gram-positive bacterial cell wall. Such Gram-positive bacteria are major causative agents of bone and soft tissue infections. The possible use of vancomycinIDRye800CW to specifically target and detect infections caused by Gram-positive bacteria has been previously shown in preclinical experiments.
In this study, we evaluated the specificity and sensitivity of vancomycin-IDRye800CW in presumably infected patient materials obtained after surgery. Our first results show that vancomycin-IDRye800CW is a specific and effective tracer to detect the presence of gram-positive bacterial infections in implants and osteomyelitis *ex vivo*.

Culturing periprosthetic tissue in blood culture bottles results in isolation of additional microorganisms

W. van den Bijllaardt[1,2*], O.P. van der Jagt[3*], M. Peijs[2], M. Janssens[2], A.G. Buiting[2], A.Q. Reuwer[2]
*Both authors contributed equally to this manuscript.
[1]Microvida Laboratory for Microbiology, Amphia Hospital, Breda, the Netherlands; [2]Laboratory for Medical Microbiology and Immunology, Elisabeth-TweeSteden Hospital, Tilburg, the Netherlands; [3]Department of Orthopaedics,

Elisabeth-TweeSteden Hospital, Tilburg, the Netherlands

Despite low sensitivity, culture of periprosthetic tissue (PPT) specimens on agars and in broths has traditionally been used for the detection of pathogens in patients suspected for prosthetic joint infection (PJI). Recent studies demonstrate a higher sensitivity of culture after additional inoculation of PPT specimens in blood culture bottles (BCBs). The aim of this study was to evaluate the added diagnostic value of culturing PPT in BCB over the conventional combination of standard agars and broths alone.

This prospective cohort study was conducted over a 12-month period and included consecutive patients undergoing revision arthroplasty. Overall, 113 episodes from 90 subjects were studied; 45 subjects (50.0%) met Infectious Diseases Society of America (IDSA) criteria for PJI, of whom the majority (75.6%) had an acute infection.

Sensitivity and specificity of culture were assessed using IDSA criteria for PJI as gold standard.

Although the sensitivity was not significantly increased, added diagnostic value of culturing PPT in BCBs was demonstrated by the significantly higher number of detected pathogens in culture sets with BCBs compared to culture without BCBs (61 pathogens in conventional set versus 89 when BCBs were included for 57 PJI episodes, $p \leq 0.0001$). In 17 (29.8%) episodes microorganisms were cultured from BCBs only and in 9 (52.9%) of these episodes virulent pathogens were found.

This study demonstrates that PPT culture in BCBs leads to isolation of additional microorganisms, both virulent and low-virulent, which were not cultured with use of agars and broths alone.

Data have been presented for a small audience in a lecture in the ETZ Tilburg on May30th and in the Diakonessenhuis Utrecht on September 19th 2018, respectively. A manuscript of the study has been submitted to a scientific journal.

Direct molecular diagnostics: sample-in-result-out testing

E. Wessels

Department of Medical Microbiology, Leiden University Medical Center, Leiden, the Netherlands

The introduction of real-time PCR has caused a revolution in diagnostic microbiology. Microorganisms that could not or hardly be cultured could be detected by real-time PCR in one day. The Leiden University Medical Center (LUMC) has an extensive portfolio of diagnostic real-time PCR applications, covering more than 100 targets. The amount of molecular diagnostic results increased every year and in 2017 more than 150,000 results were produced at the department of Medical Microbiology of the LUMC. To be able to handle these great amount of samples and results, most of the molecular diagnostic laboratories have automated the lab developed test (LDT) workflow of molecular diagnostics. At the moment we are in the transition period of the EU regulation on in vitro diagnostic medical devices that was adopted in 2017. According to that regulation laboratories should use CE-IVD assays if available for the target patient group at the appropriate level of performance. In the presentation the CE-IVD sample-in-result-out systems that are available at the moment or in the near future will be shown. The throughput and portfolio of some low/medium throughput sample-to-answer systems will be compared and the available random access, high throughput sample-to-answer platforms will be discussed. The need for molecular point-of-care tests (POCT) depends on your laboratory/hospital setting and recent literature about the performance and workflow of the available systems will be shown. The LUMC prefers syndromic testing for respiratory infections over POCT, since the latter is only able to detect influenza virus and RSV at the moment and the turnaround time of the syndromic testing systems is fast enough to have impact on the patient management in our setting. The available rapid syndromic testing systems are shown and some recent literature on the performance and impact of these systems will be discussed.