

MEETING ABSTRACT

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# Metabolomics in the diagnosis of sepsis

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## Introduction

Sepsis is an important cause of mortality and morbidity for preterm and hospitalized newborn babies. Today, no single test satisfies the criteria as being the ideal marker for the early diagnosis of neonatal sepsis. Analysis of the entire metabolome is a promising method for determining metabolic variations correlated with sepsis [1-6].

## Metabolomics profiling and sepsis

Works on metabolomics concerning sepsis conducted on animals and humans of different ages (newborn and adults) have recently been published and are presented

in Table 1. In septic patients compared to controls (in plasma and urine) it is possible to observe an increase of metabolites which are part of the oxidative metabolism of fatty acids (such as hydroxybutyrate, acylcarnitines and acetoacetate). Briefly stated, alterations in the glucose metabolism in critical conditions can be seen as a redistribution of glucose consumption from the mitochondrial oxidative phosphorylation to other metabolic pathways, such as the production of lactate and the pentose phosphate pathway. In the study by Fanos et al. [7] a combined approach based on both nuclear magnetic resonance (1H-NMR) and gas-chromatography-mass

**Table 1 Metabolomic studies that have analyzed the metabolic profiles of septic patients and of experimental animals (From ref. 6, mod.)**

Author	Population study	Sample	Metabolomic analysis	Metabolite alterations
Fanos et al. 2014	9 septic newborns vs 16 control newborns	Urine	GC-MS 1H NMR	Lactate, glucose, maltose, ribitol, ribonic acid, pseudo-uridine, 2,3,4 trihydroxybutyric acid, 2-ketopgluconic acid, 3,4 hydroxybutanoic acid, 3,4,5 trihydroxypentanoic acid <(GC-MS) Acetate, acetone, citrate, creatinine, glycine, lactate, lysine, glucose (1H-NMR)
Mickiewicz et al. 2013	60 septic shock vs 40 SIRS vs 40 control pediatric patients	Serum	1H-NMR	2-hydroxybutyrate, 2-hydroxyisovalerate, lactate, glucose, 2-oxoisocaproate, creatine, creatinine, histidine, and phenylalanine
Schmerler et al. 2012	74 SIRS vs 69 septic vs 16 control human adults	Blood	LC-MS/MS	Acylcarnitines and glycerophosphatidylcholines
Mickiewicz et al. 2014	39 septic shock adult patients vs 20 ICU control patients	Serum	1H-NMR	Isobutyrate, phenylalanine, 2 hydroxyisovalerate, myoinositol, acetylcarnitine, creatine, lactate, valine, arginine, methanol, glucose, glycine
Liu et al. 2010	40 septic vs control rats	Plasma	UPLC-Q-TOF-MS	Hypoxanthine, indoxyl sulfate, glucuronic acid, gluconic acid, proline, uracil, nitrotyrosine, uric acid and trihydroxy cholanoic acid
Lin et al. 2009	40 septic vs 20 control rats	Serum	1H NMR	Lactate, alanine, acetate, acetoacetate, hydroxybutyrate and formate
Izquierdo-Garcia et al. 2011	14 septic vs 14 control rats	Lung tissue, BALF and serum	1H NMR	Alanine, creatine, phosphoethanolamine and myoinositol

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spectrometry (GC-MS) techniques was used applied to neonatal infections. The study population included 25 neonates: 9 patients had a diagnosis of sepsis and 16 were healthy controls. This study showed a unique metabolic profile of the patients affected by sepsis compared to non-affected ones with a statistically significant difference between the two groups ( $p = 0.05$ ). Mickiewicz et al [8] examined serum samples collected from 60 patients with septic shock (by Gram- and/or Gram+), 40 patients with SIRS and 40 healthy children by nuclear magnetic resonance spectroscopy spectra. Some of the metabolite concentrations were able to separate between patient groups. The main messages from the published studies are as follows. a) Metabolomics is able to early diagnose the infection (in some cases in preclinical conditions). b) Metabolomics is able to predict the outcome in single individuals and the AUC values are close to 1. c) Metabolomics appears to be a promising and useful instrument also in the diagnosis of sepsis. d) In the next future some easy tools, like urinary dipsticks, with the discriminant metabolites will be available in clinical settings, bedside.

## Conclusions

Present-day methods and procedures for the diagnosis of systemic neonatal infections are hindered by low sensitivity and long response times. Metabolomics is showing promise of becoming a most effective method, even in neonatology and paediatrics.

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