

# Studying organ crosstalk leads to a deeper understanding of sepsis

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Sepsis, a complex systemic response to infection leading to organ failure, is generally studied at the level of individual organs; this research has hinted at altered metabolic changes. A new study in the *American Journal of Pathology* takes a two-pronged approach and investigates for the first time the metabolic changes across affected organs in a large animal model of sepsis and identifies both potential common and organ-specific metabolic alterations contributing to the disease process.

Lead investigator Monte S. Willis, MD, Ph.D., MBA, Co-Director of the Indiana Center for Musculoskeletal Health; Vice-Chair of Research, Department of Pathology and Laboratory Medicine; and Professor, Krannert Institute of Cardiology, at the Indiana University School of Medicine, Indianapolis, IN, USA, describes sepsis as "an inter-organ network issue."

"Part of the issue with improving sepsis outcomes is due to our limited understanding of the pathological process," explains Dr. Willis. "While the metabolic crosstalk of organs is taught conceptually, we tend to think of diseases in an organ-specific manner. We need to go beyond treatments that just target symptoms. Our studies illustrate that a broader system view of disease is needed and that metabolic intermediates may be responsible regulators of sepsis and other diseases."

In this study, pigs were infected with *Pseudomonas aeruginosa* (*P. aeruginosa*), a common bacterium found in soil, water, and plants. Individuals can become ill from eating *P. aeruginosa*-contaminated food

or touching infected moist areas or improperly cleaned medical equipment. Eighteen hours after infection, investigators analyzed [tissue samples](#) from the pigs' intestine, skeletal muscle, liver, and lungs to determine how specific metabolic pathways were affected across organs.

Researchers identified both common metabolic alterations and organ-specific changes in a wider range of metabolic processes than previously reported. Organ-specific deficits in metabolism were also identified, with potential therapeutic implications.

"The observed organ-specific metabolic alterations provide clues to previously unexplored mechanisms of disease, while common metabolic alterations illustrate a broader array of changes than previously reported in individual organ studies. These studies provide insight into the potential for cross-communication among tissues in system disease and how specific organ damage may require therapeutic interventions targeting metabolism," notes first author Amro Ilaiwy, MD, of the Sarah W. Stedman Nutrition and Metabolism Center, Duke Molecular Physiology Institute, Duke University Medical Center, Durham, NC, USA.

Dr. Willis and his co-investigators emphasize the need to understand disease processes as a network of communicating organs instead of focusing on an isolated organ. Given a basic acceptance of metabolic crosstalk in diseases such as diabetes, there is a basis for expanding these concepts into other complex diseases in other disciplines, such as [skeletal muscle](#) and the heart.

An estimated 1.7 million US adults develop [sepsis](#) annually, resulting in almost 270,000 deaths. Sepsis produces complex hemodynamic and cellular changes including tissue damage and [organ failure](#), leading to inadequate oxygen delivery to cells. Treatments generally target symptoms such as [low blood pressure](#) or the bacteria responsible for

infection, but do not address the underlying pathophysiology that occurs in affected organs. Understanding the underlying pathophysiology occurring in affected organs has been a challenge. Some scientists believe that progress may have been somewhat stymied by approaches that either focus too narrowly on individual organs or aim too broadly at detecting widespread [metabolic changes](#).

**More information:** Amro Ilaiwy et al, Identification of Metabolic Changes in Ileum, Jejunum, Skeletal Muscle, Liver, and Lung in a Continuous I.V. *Pseudomonas aeruginosa* Model of Sepsis Using Nontargeted Metabolomics Analysis, *The American Journal of Pathology* (2019). [DOI: 10.1016/j.ajpath.2019.05.021](https://doi.org/10.1016/j.ajpath.2019.05.021)

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