

# From heart to gut: Exploring the gut microbiome in congenital heart disease

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# Introduction

**Congenital heart disease (CHD) is a common birth defect. Despite advances in treatment techniques, children with CHD still face challenges such as neurodevelopmental disability and immune system dysfunction.**

## **Gut Microbiome and Host Interaction**

The gut microbiome, with its vast quantity, plays a crucial role in maintaining homeostasis, participating in the development of physiological systems, and influencing pathological conditions such as intestinal barrier dysfunction and systemic inflammation.

## **Relationship between Gut Microbiome and Congenital Heart Disease**

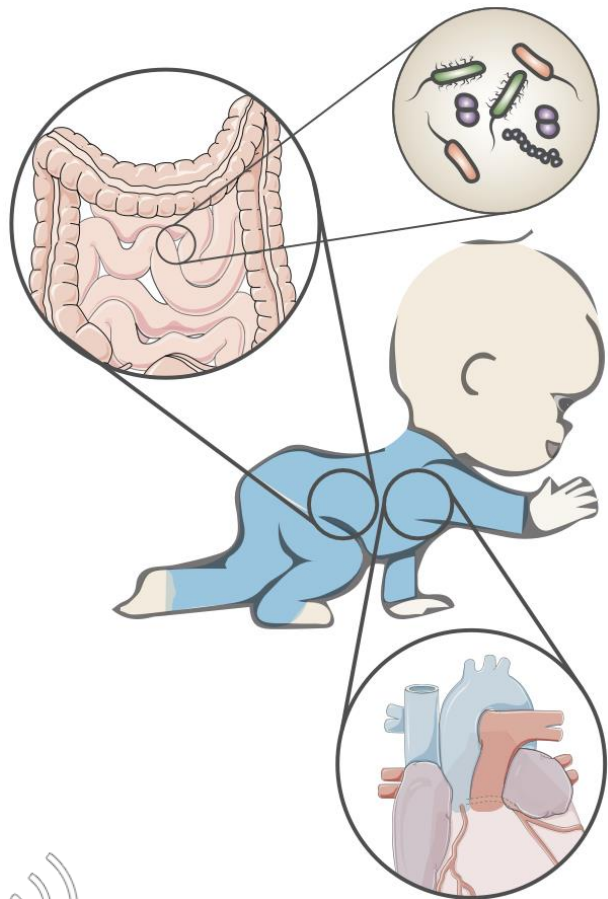
Abnormalities in the gut microbiome of children with critical congenital heart disease are associated with unfavorable clinical outcomes. Characteristics of congenital heart disease, such as chronic hypoxia, are also correlated with changes in the microbiome.

## **Role of Gut Microbiome in Pediatric Immunity, Intestinal Barrier, and Neurodevelopment**

Research underscores the importance of the gut microbiome in host metabolism and immune balance, including its role in the growth and the perioperative period of heart surgery (pediatric ICU).

## **Focus and Future Directions of Research**

The gut microbiome plays a critical role in congenital heart disease, highlighting the importance of further studying the associated mechanisms and potential therapeutic measures.



# Congenital heart disease leads to long-term chronic hypoxia and low perfusion in the intestines.

**Chronic hypoxia is a characteristic feature of cyanotic congenital heart disease, and its severity depends on the type of cardiac malformation.**

## The Relationship between Hypoxia and Inflammation

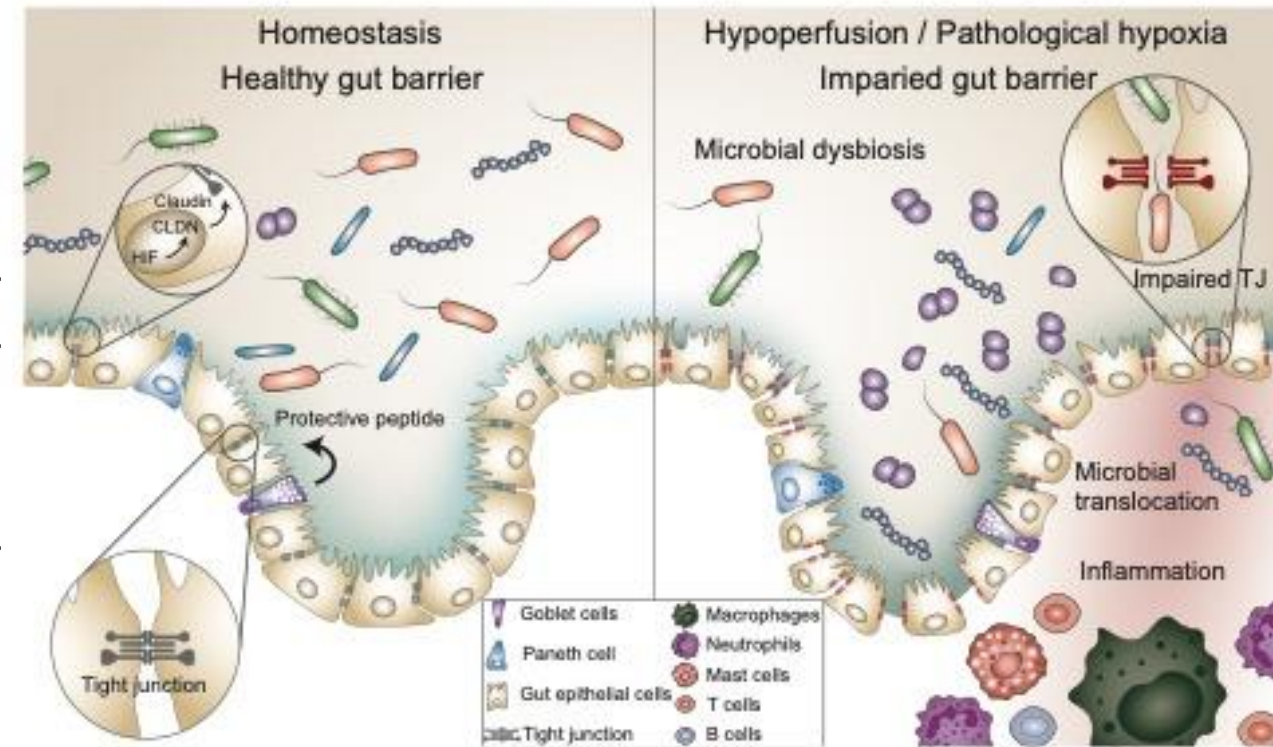
In the low-oxygen environment of the intestines, pathological hypoxia may also lead to intestinal inflammation and barrier damage.

### Hypoxia-inducible factors (HIF)

HIF plays a crucial role in the adaptive response to chronic hypoxia, regulating cardiac function and maintaining intestinal barrier integrity. Microbial metabolic products enhance intestinal barrier function by modulating HIF.

### Reduced Intestinal Perfusion and Inflammation

Reduced intestinal perfusion is a risk factor for intestinal barrier dysfunction, triggering inflammatory responses. Congenital heart disease leading to inadequate intestinal perfusion can exacerbate this phenomenon.



# Congenital heart disease and neurodevelopment

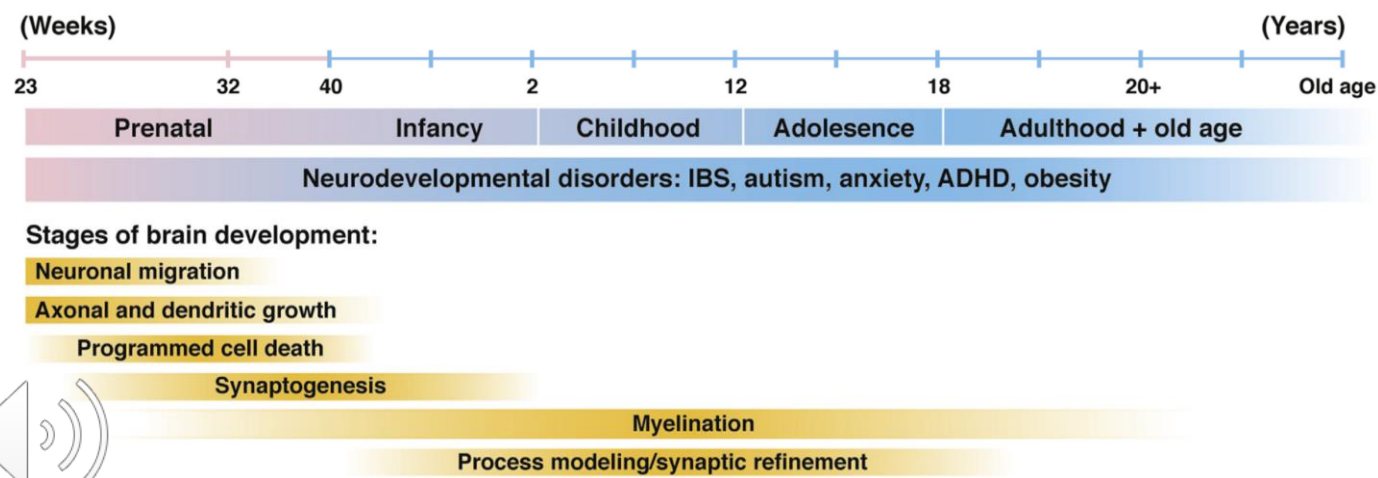
Children with congenital heart disease are prone to developing neurodevelopmental disabilities, manifested as issues in cognition, motor skills, language, and other aspects. This may be attributed to the impact of the circulatory abnormalities associated with congenital heart disease on fetal brain blood supply and delayed brain development. Additionally, children with congenital heart disease are more susceptible to acquired white matter injury, especially when there are risk factors such as premature birth, hypoxia, and prolonged surgeries.

## The gut microbiome and blood-brain barrier dysfunction

The gut microbiome can influence the integrity of the blood-brain barrier by affecting cytokines or through the production of metabolic products. This may be associated with neurodevelopmental disabilities in children with congenital heart disease.

## Neuroimmune System and Gut Microbiome

The gut microbiome can influence the development of fetal microglial cells, and at the same time, its metabolites also impact the maturation and function of microglial cells.



# Cardiovascular surgery and the gut microbiome

**Cardiovascular surgery has a significant impact on the gut microbiome, potentially involving an increase in pathogenic bacteria and a decrease in short-chain fatty acid-producing bacteria. The imbalance in this microbial community is associated with patients' clinical characteristics and susceptibility to postoperative complications, such as acute kidney injury**

## **Use of Cardiopulmonary Bypass**

Cardiopulmonary bypass is a crucial approach employed in cardiac surgery but may lead to an imbalance in the gut microbiome and a systemic inflammatory state. Certain metabolites produced by the gut microbiome have a protective effect against the damage caused by cardiopulmonary bypass, such as the role of short-chain fatty acids in alleviating ischemia-reperfusion injury in the heart.

## **Dysbiosis in Gut Microbiome**

Cardiopulmonary bypass may induce local and systemic inflammation in the gut, which is associated with adverse outcomes following cardiac surgery. Disruption of the gut barrier and compromised tight junctions in the intestinal epithelium may already exist before congenital heart surgery and further worsen during the systemic inflammatory process induced by cardiopulmonary bypass.

## **Abnormal Gut Barrier Post-Congenital Heart Surgery**

Post-congenital heart surgery, pediatric patients may exhibit abnormally increased intestinal permeability, potentially leading to postoperative endotoxemia, systemic inflammation, and organ dysfunction.

## **Impact of Antibiotics on Gut Microbiome**

Postoperative antibiotic use may reduce the richness and diversity of the gut microbiome, increasing the relative abundance of specific bacteria.

**In summary, the interplay between cardiovascular surgery and the gut microbiome is complex, involving aspects such as inflammation, metabolism, and gut permeability. Further research is needed to understand these intricate interactions.**



# Summary (research gaps and therapeutic potentials)

**Despite numerous studies revealing the crucial role of the gut microbiome in cardiovascular diseases, evidence in congenital heart disease remains limited.**

The exact roles of microbial communities in other parts of the body, including oral and maternal microbiome, in the occurrence and development of congenital heart disease are not well-defined.

The direct impact of microbial metabolites on various aspects of congenital heart disease, including children's physical growth and development, neurodevelopment, and immune development, is significant.

## **Exploring Therapeutic Potential**

Utilizing techniques such as metabolomics for personalized analysis of the gut microbiome can guide the optimization of perioperative management for children with congenital heart disease. Investigating perioperative nutritional strategies to alter the gut microbiome and accelerate patient recovery may become a complementary approach to postoperative rehabilitation. Other methods, such as fecal microbiome transplantation, may contribute to reshaping the ecological balance of the gut microbiome.

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