Maternal antibiotic treatment may harm preemies' lungs

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New research in mice suggests that exposure to antibiotics before birth may impair lung development in premature infants. The study, the first to explore the gut-lung axis in prematurity, is published ahead of print in the *American Journal of Physiology*—Lung Cellular and Molecular Physiology and was chosen as an APSselect article for December.

Premature infants, particularly those who receive oxygen treatment soon after birth, are at high risk of developing lung problems characterized by scarring (fibrosis) and inflammation. Emerging research suggests that the communities of bacteria in the digestive tract (gut microbiome) can impair development of the immune system and may also affect inflammation, which in turn plays an important role in lung disease. The interaction among these body systems is called the gut-lung axis. Antibiotics are known to change the makeup of the gut microbiome and are linked to an increased risk of lung injury. Antibiotic treatment is common in premature babies, but how the gut is involved is not clear. Looking at how antibiotics affect offspring—even before birth—may help researchers better understand the gut-lung axis.

In a new study, researchers exposed one group of pregnant mice to the widely used antibiotic penicillin in their drinking water ("treated dams"). Another group of pregnant mice received plain water ("control dams"). After the babies were born, the research team used a cross-over experimental model to assess the effects of antibiotics on the offspring in combination with oxygen treatment. They looked at four groups:

- One group was exposed to penicillin before birth and was fed by treated dams.
- One group was exposed to penicillin before birth and was fed by control dams.
- One group was not exposed before birth and was fed by treated dams.
- One group was not exposed before birth and was fed by control dams.

The research team examined lung structure, including thickness of the walls, size of capillaries and scar tissue—together all of these affect breathing ability. They also looked at the inflammation-causing cells and proteins in the lungs of all the animals.

Mice that were exposed to antibiotics before birth and fed by control dams had more fibrosis with oxygen treatment than mice exposed to antibiotics only after birth. Offspring exposed to penicillin in the womb also had lower body mass and reduced capillary size compared with those not exposed before birth. Prenatal exposure also altered levels of proteins that promote inflammation and immune function as well as those that affect microbial signaling in the lungs.

"Our study provides valuable experimental evidence that manipulation of the gut microbiota by antibiotic exposure influences the progression of lung injury," the researchers wrote. These findings "may assist in the interpretation of future observational studies in human newborns examining the role of the gut-lung axis in

[bronchopulmonary dysplasia]."

More information: Kent A Willis et al. Perinatal maternal antibiotic exposure augments lung injury in offspring in experimental bronchopulmonary dysplasia, *American Journal of Physiology-Lung Cellular and Molecular Physiology* (2019). DOI: 10.1152/ajplung.00561.2018

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