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The placental microbiome and pediatric research

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The Human Microbiome Project has been underway since 2008, and the microbiome itself is haltingly making its way into the mainstream news. The human microbiome is the vast mosaic of microbes living on and inside the human body: the ears, tongue, cheeks, gut, nose, skin, vagina, and stool each host populations of archaea and bacteria. A cascade of new observations links any piece of this puzzle to different conditions in health and disease.

As an example, rheumatoid arthritis–related autoimmunity may be initiated at a mucosal site years before the onset of joint symptoms (1). The candidate sites of origin include the oral, lung, and gastrointestinal mucosa. Moreover, autoimmunity and inflammation are not limited to specific rheumatologic and inflammatory disorders, but represent a driving force in the pathogenesis of cardiovascular and metabolic diseases. Accordingly, the relations among gut microbiota, energy homeostasis, and inflammation, as well as their roles in obesity-related disorders, are increasingly recognized (2).

The possibilities for future research surrounding the microbiome abound, from examining its role in nutrition and asthma to the possibility of microbiota transplants. Now, there is yet another frontier to investigate: the placenta.

The once-prevailing theory that human fetuses grow in a sterile womb and only acquire bacteria during and after birth has been in doubt for the past several years (3). Most animals transmit maternal bacteria to offspring (4); and after over a century of believing the human womb to be bacteria-free, researchers have found that human mothers do in fact transmit bacteria to their children through the placenta (5). Aagaard *et al.* recently published their preliminary research on the placental microbiome in *Science Translational Medicine*. The article sketches out the taxonomy of the placental microbiome and points out discrepancies that may be associated with preterm birth.

For the study, researchers studied 320 placental specimens. Despite expected differences between individuals, the taxonomic classification of the placental microbiome bears most similarity to the nonpregnant oral microbiome. In fact, the tongue, tonsils, saliva, throat, and plaque all have microbes in common with the placenta. *Escherichia coli* was found to be the most prevalent species in the placenta, which, however, is not the case in the oral microbiome.

Aagaard *et al.* also compared placental specimens from healthy births to births that involved complications. There were two case cohorts: cases of preterm birth and cases of remote history of antenatal infection. They found that placentas from normal deliveries and preterm deliveries contained different populations of microbial species. The study had several limitations, including the infeasibility of investigating the placental microbiome in early gestation among women who deliver at term (6). However, as a preliminary study, it posits ideas for further research.

The discovery of the microbiome has greatly animated the medical community, and the placental microbiome offers still more opportunities for exploration. Why are the oral and placental microbiomes so similar? Could the placental microbiome make a difference in antenatal infection? Does exposure to antibiotics during pregnancy significantly change the placental microbiome, and how does a caesarean section affect the interaction between it and the infant?

Watch for the 2015 Annual Review Issue of *Pediatric Research*, scheduled for January. The topic is "Nutrition and the microbiome," and papers include research on the effects of the maternal microbiome, prebiotics, probiotics, human milk, dysbiosis, and the infant gut microbiome on human health and disease. The role of the microbiome in the processes of cell control among the splanchnic organs and the central nervous system will be stressed, suggesting a new and fascinating view on symbiosis between humans and inhabitant bacteria.

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