

PCBs Increase Inflammation, Disrupt Gut Microbiome, and Alter Metabolism

Researchers have discovered that exposure to certain polychlorinated biphenyls (PCBs) can increase inflammation in the intestines, alter normal gut microbiota, and disrupt metabolism. They suggest that some of the observed health impacts of PCBs may be initiated in the gut, and that changes in the gut microbiota may offer a marker for pollutant exposures.

PCBs, used in insulation, coolants, and in electrical equipment until 1997, are persistent in the environment and are known to harm human health. In particular, they are linked to increased risk of cardiometabolic diseases, like diabetes and heart disease.

Because people are often exposed to PCBs through contaminated food, researchers led by Jessie Hoffman, Mike Petriello, Ph.D., and Bernhard Hennig, Ph.D., of the University of Kentucky Superfund Research Program (SRP) Center, sought to identify the effect of exposure to a specific type of PCB, known as PCB 126, on gut microbiota. Gut microbiota play an important role in metabolism, immune function, and overall health.

The team used mice lacking genes for low-density lipoprotein receptors, which help regulate the amount of cholesterol in the blood, and fed them a high cholesterol diet to represent a model of cardiometabolic disease. The research team previously showed that PCB 126 could accelerate heart disease and increase inflammation throughout the body in this particular mouse model.

Using a combination of RNA gene sequencing, metabolomics, and mathematical modeling, they examined the impacts of PCB exposure on gut microbiota, intestinal inflammation, and metabolism.

Microbiota in the gut are known to be sensitive to diet and exposure to some harmful pollutants. To explore the impact on microbiota as a result of PCB 126 exposure, the researchers analyzed intestinal and fecal samples over time.

The team found that PCB exposure changed gut microbiota populations and decreased their diversity. PCB 126-exposed mice had lower microbial diversity, richness, and distribution, compared to untreated mice. They also observed decreases in some health-promoting bacteria, such as *Lactobacillus* and *Bifidobacteria*.

According to the authors, some of the changes observed in PCB-exposed mice were similar to those observed in humans with various metabolic disorders or inflammatory diseases. For example, they reported an increase in the ratio of *Firmicutes* to *Bacteroidetes* microbiota, which has been previously reported to be linked to increased risk of infection, inflammation, and insulin resistance. The trends in bacterial alterations were noted to be similar to what is observed in humans with irritable bowel syndrome or type two diabetes.

Because intestinal inflammation is known to be a risk factor for cardiometabolic diseases, the researchers also examined markers of inflammation in the small and large intestines.

The team found that PCB 126 exposed mice had measurable PCB 126 in the colon and higher expression of the gene *Cyp1a1*, which indicates activation of a gene which plays an important role in detecting and responding to certain pollutants. According to the authors, the elevated

Cyp1a1 observed long after oral PCB exposure ended may indicate that PCBs are recirculated between the liver and the intestines, leading to chronic inflammation in the gut.

In PCB exposed mice compared to untreated mice, they also found increased expression of inflammatory cytokines, which are small proteins that are important in immune cell signaling. According to the authors, the observed markers indicate that PCB exposure can trigger an inflammatory response not only locally in the intestines, but throughout the body.

Using metabolomics approaches, the team examined the influence of PCB exposure on several processes related to the metabolic function of the liver. According to the authors, the changes observed in PCB-exposed mice were similar to those observed in metabolic diseases, such as a shift towards fatty acid metabolism, which is more common with diabetics.

PCB 126 exposure also increased several indicators of cardiometabolic disease, such as increased insulin and increased fasting blood glucose levels, compared to unexposed mice. These observations were further supported by reported decreases in the peptide GLP-1, which is important in managing insulin levels, in PCB treated mice. According to the authors, the high level of inflammation observed in PCB exposed mice may be responsible for the dysregulation of insulin signaling.

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