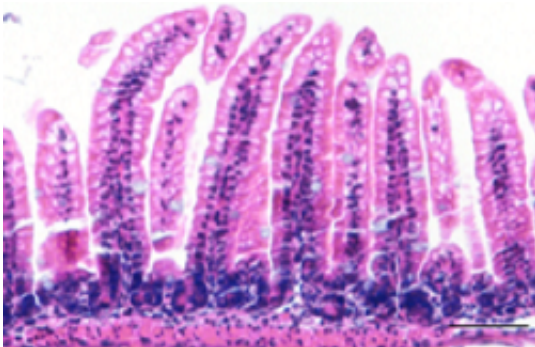


Vitamin A quells severity of preemie GI disease in mice

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Tissue from a healthy mouse intestine are shown. Credit: *Journal of Clinical Investigation*

After observing that some gastrointestinal disease in premature human and mouse infants progresses only when certain immune system white blood cells go into inflammatory overdrive, Johns Hopkins researchers have found that giving large doses of vitamin A to mice converts those blood cells into inflammation suppressors and reduces the severity of the disease, compared to untreated mice.

The findings, which add to evidence of vitamin A's anti-inflammatory properties, are published online Dec. 21 in the *Journal of Clinical Investigation*.

An estimated 5 to 10 percent of premature babies develop a severe form

of bowel disease called necrotizing enterocolitis, an inflammatory condition marked by the death of intestinal tissue and lifelong digestive, lung and other impairments, if they survive. One in four infants who get the disease will die from it.

"It's amazing and maybe a little humbling to think that a naturally occurring vitamin might put out the fire of such a devastating disease," says David Hackam, M.D., Ph.D., surgeon-in-chief at the Johns Hopkins Children's Center and professor of surgery at the Johns Hopkins University School of Medicine. "It's a nasty disease for which there isn't reliable treatment, and certainly no specific cure."

Hackam cautions that the safety of high doses of vitamin A in children is not yet established and that additional studies must be performed before such therapy would be available to infants. That could take several years, he says.

For the study, Hackam and his team first analyzed the types of white blood [cells](#) in the intestines of human infants and newborn [mice](#) with the rodent form of the disease, focusing on the large number of T cells they found there.

Using newborn mice genetically engineered to lack T cells, they introduced gut bacteria from mice with the disease and established that mice without T cells failed to develop the condition. But when T cells taken from diseased mice were given to newborn mice without T cells, the same genetically engineered mice acquired the disease.

Of the T cells analyzed from diseased intestines, they found the majority consisted of inflammatory T cells—of the type CD4+ Th17—and few inflammation suppressor cells, known as Tregs. In an unrelated study from the La Jolla Institute for Allergy and Immunology, investigators showed that retinoic acid, a compound derived from vitamin A, reduced

the level of inflammatory T cells and increased the level of inflammation suppressor T cells.

The researchers used this knowledge to test whether changing the balance of the T cells would reduce the severity of the disease in mice with necrotizing enterocolitis. They fed the mice 50 micrograms of vitamin A daily for four days, considered a fairly low dose. When they looked at the intestines of the diseased mice fed vitamin A, they looked more like healthy intestines than diseased ones.

Hackam says further experiments revealed that cells in the intestinal lining contain a bacteria-sensing receptor on their surface responsible for attracting swarms of inflammatory T cells to the intestines; [intestinal cells](#) without the receptor—called toll-like receptor 4, or TLR4—failed to draw in the inflammatory T cells.

To learn if the inflammatory T cells caused physical damage to the intestinal cells, the researchers added a protein released by the inflammatory T cells to laboratory-grown mouse intestinal tissue and to the [intestinal tissue](#) of disease-free newborn mice. Intestinal cells with the T cell protein died more often and produced fewer new intestine cells than [healthy cells](#) both in the lab-grown cultures and in the newborn mice.

"This interaction between the T cells and the intestine seems to feed the fire in developing the disease," says Hackam.

Provided by Johns Hopkins University School of Medicine

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