'Pouchitis' after ulcerative colitis surgery linked to changes in gene expression

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"Pouchitis" developing after surgery for ulcerative colitis (UC) is associated with changes in gene expression, which increase along with disease severity, reports a study in *Inflammatory Bowel Diseases*, official journal of the Crohn's & Colitis Foundation of America (CCFA).

"Gene alterations in pouch inflammation and Crohn's disease overlap, suggesting that inflammatory bowel disease is a spectrum, rather than distinct diseases," according to the new research by Dr S. Ben Shachar and colleagues of Tel Aviv University, Israel. They believe the occurrence and progression of gene changes in previously normal intestine after UC surgery provides a useful model for studying the development of inflammatory bowel disease (IBD).

After UC Surgery, Gene Expression Changes in Patients with "Pouchitis"

The researchers analyzed gene expression changes in different groups of patients who had undergone "pouch" surgery for UC. In this procedure (restorative proctocolectomy), the entire large intestine is removed and a portion of small intestine (the ileum) is used to create a reservoir, or pouch, to restore bowel function.

Up to one-fourth of patients with UC need surgery because of unmanageable disease or complications. Surgery is effective, but has a substantial rate of complications—especially the development of

inflammation in the newly created pouch, called pouchitis.

By definition, the small intestine is normal in UC—in contrast to Crohn's disease (CD), which can affect any part of the gastrointestinal tract. The development of pouchitis after UC surgery thus provides an opportunity to study the "molecular events" associated with the development of IBD in previously normal tissue.

The researchers found no significant changes in gene expression in normal samples of ileum from patients with UC. In contrast, in patients who had undergone UC surgery, nearly 170 significant changes in gene expression were found in samples of tissue from the surgically created pouch—even though the tissue still appeared normal.

In patients who had developed inflammation and other signs of pouchitis, the number of gene abnormalities increased to nearly 500. For those who progressed to develop "Crohn's-like" changes of the pouch tissue, the number of gene abnormalities increased to well over 1,000. Thus as the severity of pouch disease increased, so did the number of gene expression changes.

Overlapping Gene Alterations Linked to Increasing Inflammation

The types of gene expression changes overlapped significantly between groups. The alterations involved genes involved in a wide range of inflammatory processes, including responses to chemical stimuli, various metabolic and immune system processes, and pathways related to certain types of infections. The link to infectious processes might help to explain why IBD and pouchitis often respond well to treatment with antibiotics.

Since the number and extent of gene expression changes build up as pouchitis progresses, "molecular clustering" studies might be a useful part of clinical assessment for IBD, according to Dr Shachar and coauthors. The findings also suggest that pouchitis—especially Crohn's-like changes—may not be a separate different disease, "but rather the end of the IBD spectrum."

Perhaps most importantly, the development of pouchitis may provide a unique model for understanding how IBD develops and progresses. Dr Shachar and colleagues write, "We suggest that the pouch can serve for study of early IBD in humans, with the ultimate goals of tailoring intervention and devising strategies for prevention."

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